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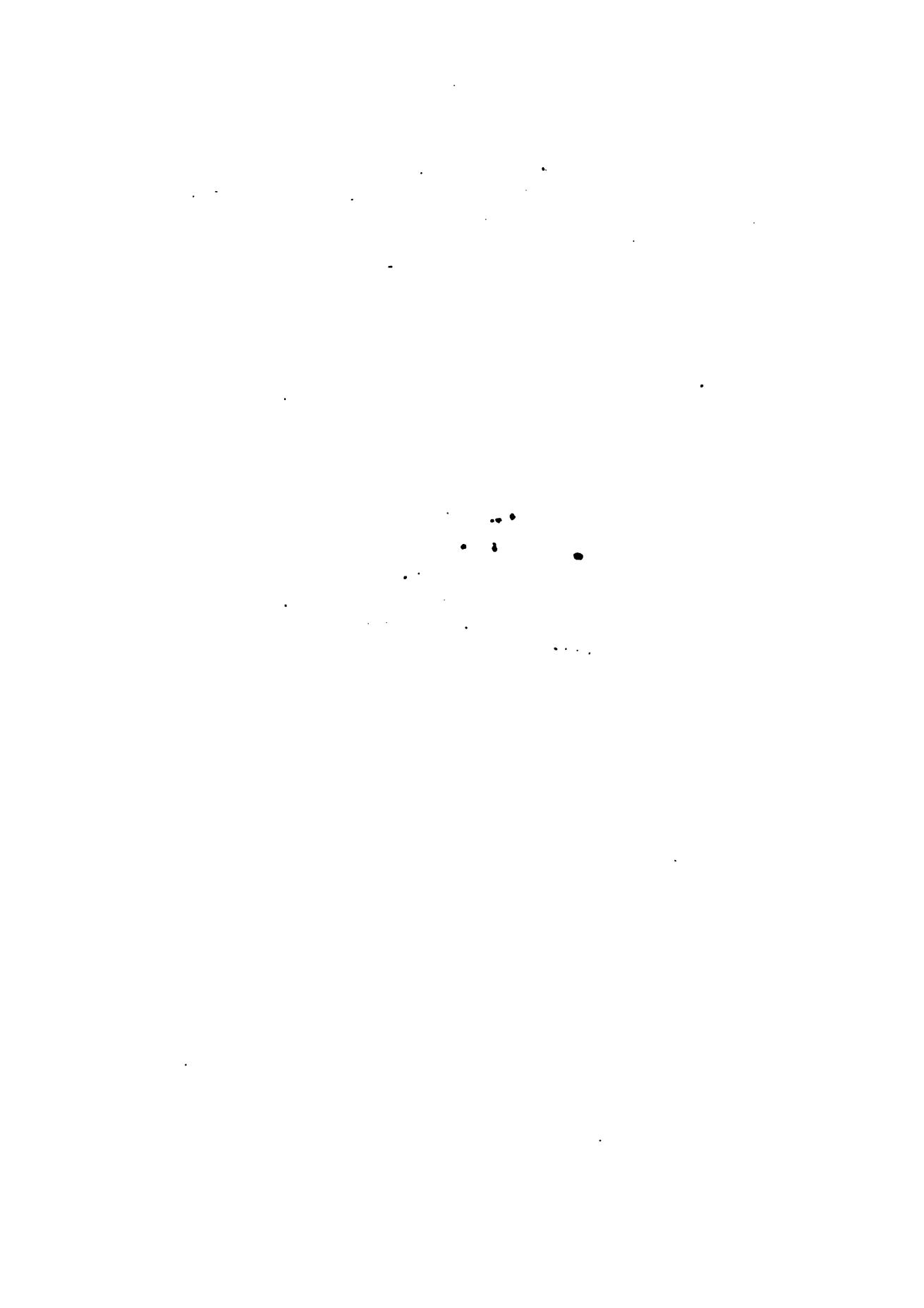
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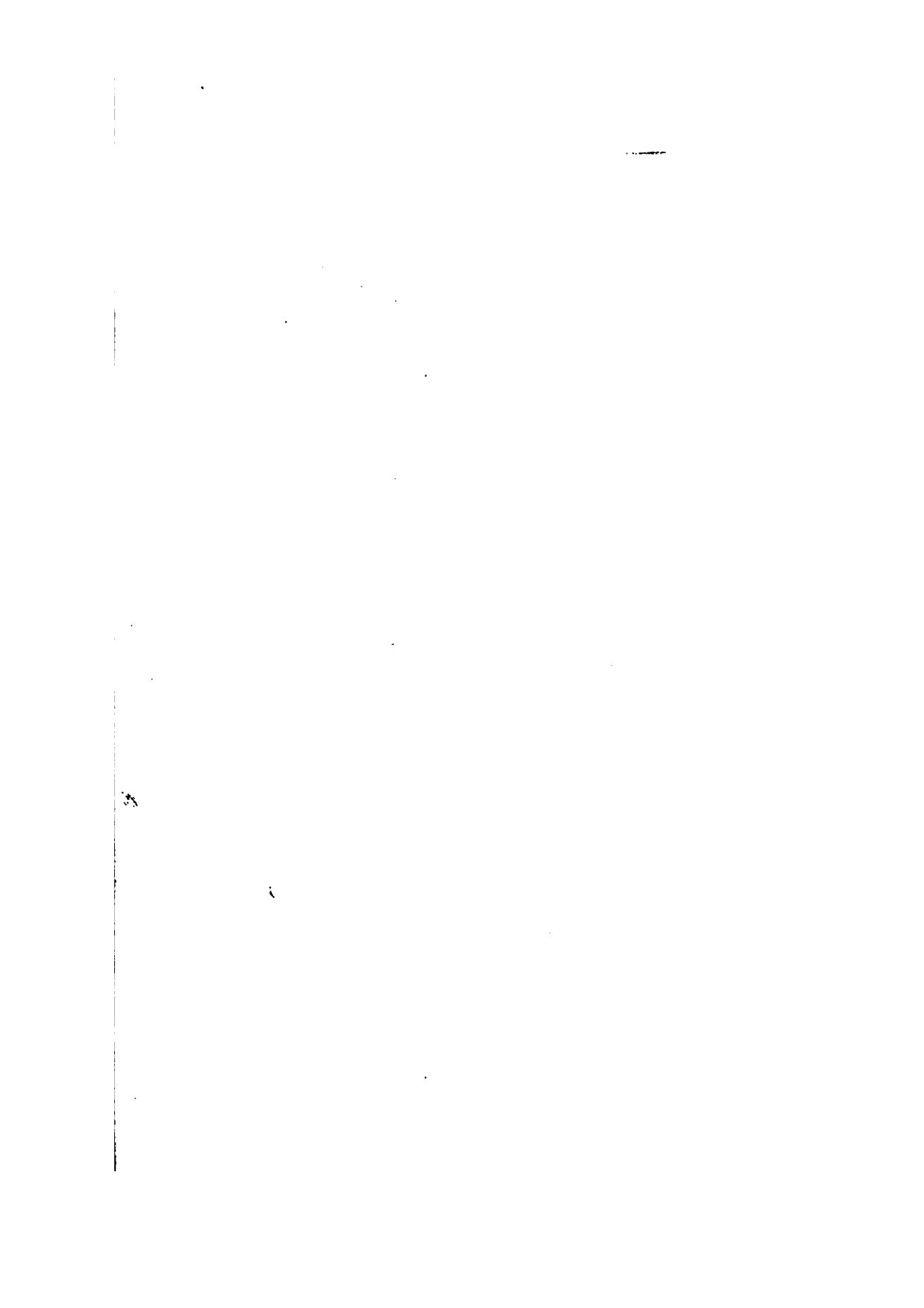
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POISONS

THEIR EFFECTS AND DETECTION

A MANUAL FOR THE USE OF ANALYTICAL
CHEMISTS AND EXPERTS

*WITH AN INTRODUCTORY ESSAY ON THE GROWTH OF MODERN
TOXICOLOGY*

BY

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PUBLIC ANALYST FOR ST. MARYLEBONE

With Tables and Illustrations

VOLUME I



NEW YORK
WILLIAM WOOD & COMPANY
56 & 58 LAFAYETTE PLACE

1885



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P R E F A C E.

THE present Volume completes an entirely rewritten and greatly enlarged Second Edition of the Author's "*Practical Chemistry*." The reasons for the change of title have been already explained in the preface to Vol. I., the volume on "*Foods*."

In both Manuals—"Foods" and "Poisons"—a common mode of introducing the subject by an historical notice has been adopted ;—in the one case, successive methods of Food-Adulteration were briefly sketched, and, in the other, the forms of poisoning practiced by different nations at different periods, together with the growth of modern Toxicology, have been passed under review.

The primary object in the Classification followed is the convenience of the Practical Chemist ; but, wherever possible, "natural" groups of Poisons have been formed.

Snake-poison and other toxic Animal Secretions have received notice, and much attention has been paid to a subject comparatively unworked —that of the Cadaveric Alkaloids.

In the Appendix will be found a brief *résumé* of the latest methods for the identification of Stains of Blood : and, for immediate reference in cases of emergency, it has been thought advisable to add an alphabetically-arranged List of the more common Poisons, with brief directions for treatment.

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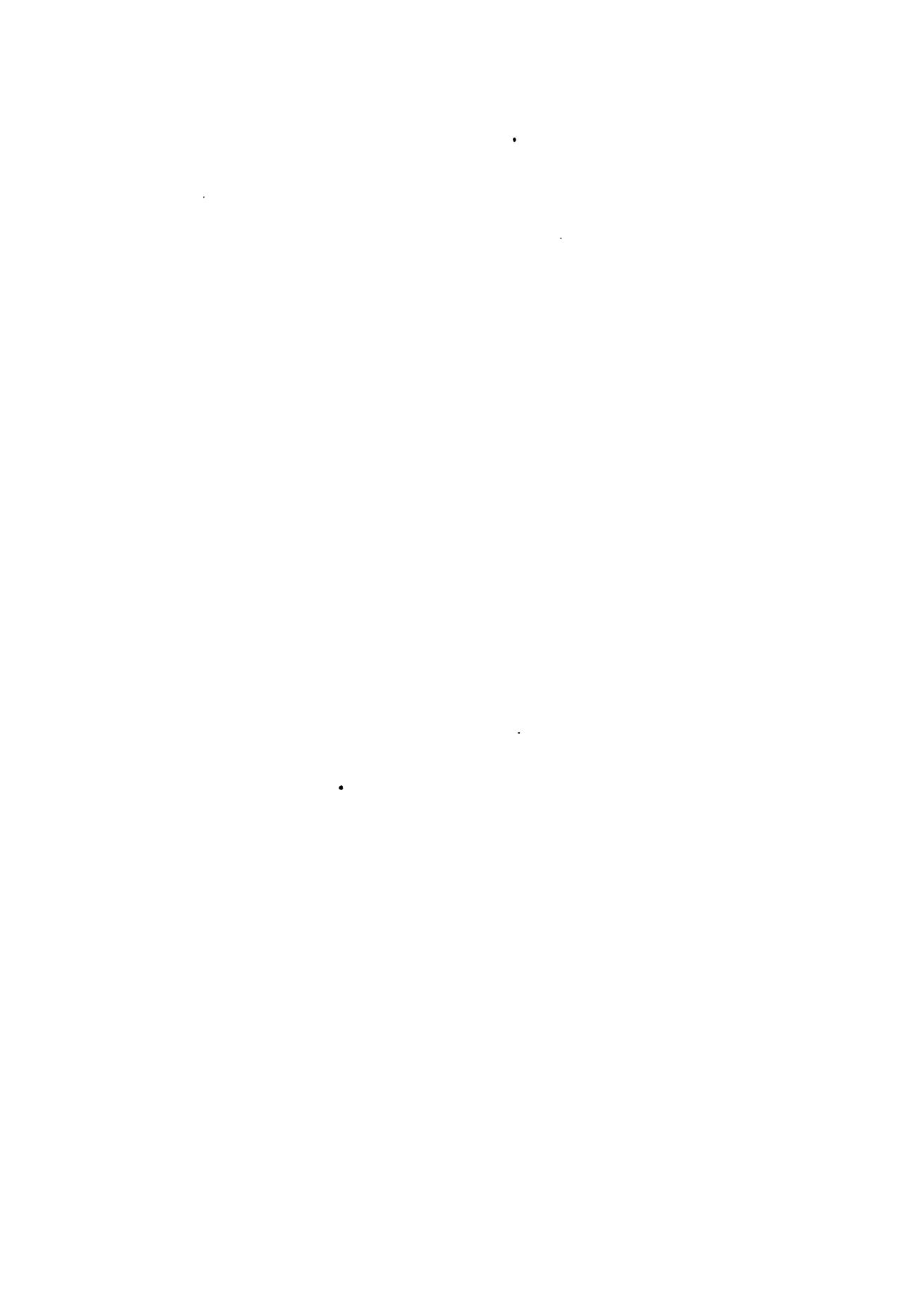
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POISONS

THEIR EFFECTS AND DETECTION.

PART I.—INTRODUCTORY.

I.—THE OLD POISON-LORE.

It is significant that the root “*tox*” of the modern word *toxicology* can be traced back to a very ancient word meaning “bow” or “arrow,” or, in its broadest sense, some “tool” used for slaying: hence it is no far-fetched supposition that the first poison-knowledge was that of the septic poisons. Perchance the savage found that weapons soiled with the blood of former victims made wounds fatal; from this observation, the next step naturally would be that of experiment,—the arrow or spear would be steeped in all manner of offensive pastes, and smeared with the vegetable juices of those plants which were deemed noxious; and as the effects were mysterious, they would be ascribed to the supernatural powers, and covered with a veil of superstition.

The history of the *poison-lehre*, like all history, begins in the region of the myths; there was a dark saga prevailing in Greece, that in the far North existed a land ruled by sorcerers—all children of the sun—and named Aeëtes, Perses, Hecate, Medea, and Circe. Later on, the enchanted land was localised at Colchis, and Aeëtes and Perses were then said to be brothers. Hecate was the daughter of Perses; she was married to Aeëtes, and their daughters were Medea and Circe.

Hecate was the discoverer of poisonous herbs, and learned in remedies both evil and good. Her knowledge passed to Medea, who narcotised the dragon, the guardian of the golden fleece, and incited Jason to great undertakings.

In the expedition of the Argonauts, the poets loved to describe Hecate's garden, with its lofty walls. Thrice-folding doors of ebony barred the entrance, which was guarded by terrible forms; only the initiated few, only they who bore the leavened rod of expiation, and the concealed conciliatory offering of the Medea, could enter into the sanctuary. Towering above all was the temple of the dread Hecate, whose priestesses offered to the gods ghastly sacrifices.

The oldest Egyptian king, Menes, and Attalus Phylometer, the last king of Pergamus, were both famous for their knowledge of plants. Attalus Phylometer was acquainted with *hyoscyamus*, *aconite*, *conium*, *veratrum*, and others; he experimented on the preparation of poisons, and occupied himself in compounding medicines. Mithradetes Eupator stood yet higher; the receipt for the famous *theriaca*, prepared in later years at an enormous price, and composed of fifty-four different ingredients, is ascribed to him. The wonderful skill shown by the Egyptians in embalming and technical works, is sufficient to render it fairly certain that their chemical knowledge was considerable; and the frequent operations of one caste upon the dead must have laid the foundations of a pathological and anatomical culture, of which only traces remain.

The Egyptians knew prussic acid, as extracted in a dilute state from certain plants, among the chief of which was certainly the peach—on a papyrus preserved at the Louvre, M. Duteil read, “Pronounce not the name of I. A. O., under the penalty of the peach!” in which dark threat, without doubt lurks the meaning that those who revealed the religious mysteries of the priests were put to death by waters distilled from the peach. That the priests actually distilled the peach-leaves has been doubted by those who consider the art of distillation a modern invention; but this process was well known to adepts of the third and fourth centuries, and there is no inherent improbability in the supposition that the Egyptians practised it.

From the Egyptians the knowledge of the deadly drink appears to have passed to the Romans, for, although not expressly mentioned, yet the fact that, in the reign of Tiberius, a Roman knight, accused of high treason, swallowed a poison, and fell dead at the feet of the senators, is wholly inexplicable, unless it is allowed that the fatal dose was prussic acid, and that in a tolerably concentrated form.

The use of poison by the Greeks, as a means of capital punishment, without doubt favoured suicide by the same means; the easy, painless death of the state prisoner would be often preferred to the sword by one tired of life. The ancients looked indeed upon suicide, in certain instances, as something noble, and it was occasionally formally sanctioned. Thus, Valerius Maximus tells us that he saw a woman of quality, in the island of Ceos, who, having lived happily for ninety

years, obtained leave to take a poisonous draught, lest, by living longer, she should happen to have a change in her good fortune ; and, curiously enough, this sanctioning of self-destruction seems to have been copied in Europe. Mead relates that the people of Marseilles of old had a poison, kept by the public authorities, in which *cicuta* was an ingredient ; a dose was allowed to any one who could show why he should desire death. Whatever use or abuse might be made of a few violent poisons, Greek and Roman knowledge of poisons, their effects and methods of detection, was stationary, primitive, and incomplete.

Nicander of Colophon (204-138, B. C.) wrote two treatises, the most ancient works on this subject extant, the one describing the effects of snake venom ; the other, the properties of opium, henbane, certain fungi, *colchicum*, aconite and *conium*. He divided poisons into those which kill quickly, and those which act slowly. As antidotes, those medicines are recommended which excite vomiting—*e. g.*, lukewarm oil, warm water, mallow, linseed tea, &c.

Dioscorides (40-90, A. D.) well detailed the effects of cantharides, sulphate of copper, mercury, lead and arsenic. By arsenic he would appear sometimes to mean the sulphides, sometimes the white oxide. *Dioscorides* divided poisons, according to their origin, into three classes. *viz.*—

Animal Poisons.—Under this head were classed cantharides, and allied beetles, toads, salamanders, poisonous snakes, a particular variety of honey, and the blood of the ox, probably the latter in a putrid state. He also speaks of the “*sea-hare*.” The sea-hare was considered by the ancients very poisonous, and Domitian is said to have murdered Titus with it. It is supposed by naturalists to have been one of the genus *aplysia*, among the *gasteropods*. Both Pliny and *Dioscorides* depict the animal as sometimes very formidable : it was not to be looked at, far less touched. The *aplysiae* exale a very nauseous and foetid odour when they are approached : the best known of the species resembles, when in a state of repose, a mass of unformed flesh ; when in motion, it is like a common slug ; its colour is reddish-brown ; it has four horns on its head ; and the eyes, which are very small, are situated between the two hinder ones. This *aplysia* has an ink reservoir, like the *sepia*, and ejects it in order to escape from its enemies ; it inhabits the muddy bottom of the water, and lives on small crabs, *mollusca*, &c.

Poisons from Plants.—*Dioscorides* enumerates opium, black and white *hyoscyamus* (especially recognising the activity of the seeds), *mandragora*, which was probably a mixture of various *solanaceæ*, *conium* (used to poison the condemned by the people of Athens and the dwellers of ancient Massilia), *elaterin*, and the juices of a species of *euphorbia* and *apocynæe*. He also makes a special mention of aconite, the name of which is derived from *Akon*, a small city in Heraclea. The Greeks were

well aware of the deadly nature of aconite, and gave to it a mythical origin, from the foam of the dog Cerberus. Colchicum was also known to Dioscorides; its first use was ascribed to Medea. Veratrum, album and nigrum were famous medicines of the Romans, and a constituent of their "rat and mice powders;" they were also used as insecticides. According to Pliny, the Gauls dipped their arrows in a preparation of veratrum.* Daphne mezereum, called by the Romans also smilax and taxus, appears to have been used by Cativolcus, the king of the Eburones, for the purpose of suicide, or possibly by "taxus" the yew-tree is meant.†

The poisonous properties of certain fungi were also known. Nicander calls the venomous mushrooms the "evil fermentation of the earth," and prescribes the identical antidotes which we would perhaps give at the present time—viz., vinegar and alkaline carbonates.

Mineral Poisons.—Arsenic has been already alluded to. The ancients used it as a caustic and depilatory. Copper was known as sulphate and oxide; mercury only as cinnabar: lead oxides were used, and milk and olive-oil prescribed as an antidote for their poisonous properties. The *poison-lehre* for many ages was considered as something forbidden. Galen, in his treatise "On Antidotes," remarks that the only authors who dared to treat of poisons were Orpheus, Theologus, Morus, Mendesius the younger, Heliodorus of Athens, Aratus, and a few others; but none of these treatises have come down to us. From the close similarity of the amount of information in the treatises of Nicander, Dioscorides, Pliny, Galen, and Paulus *Aegineta*, it is probable that all were derived from a common source.

If we turn our attention to early Asiatic history, a very cursory glance at the sacred writings of the East will prove how soon the art of poisoning, especially in India, was used for the purpose of suicide, revenge, or robbery.

The ancient practice of the Hindoo widow—self-immolation on the burning pile of her husband—is ascribed to the necessity which the Brahmins were under of putting a stop to the crime of domestic poisoning. Every little conjugal quarrel was liable to be settled by this form of secret assassination, but such a law, as might be expected, checked the practice.

Poison was not used to remove human beings alone, for there has been from time immemorial in India much cattle-poisoning. In the institutes of Menu, it is ordained that when cattle die, the herdsman shall carry to his master their ears, their hides, their tails, the skin below their navels, their tendons, and the liquor oozing from their foreheads. Without doubt these regulations were directed against cattle-poisoners.

* Pliny xxv. 5.

† *De Bello Gallico*, vi. 31.

The poisons known to the Asiatics were arsenic, aconite, opium, and various solanaceous plants. There has been a myth floating through the ages that a poison exists which will slay, a long time after its introduction. All modern authors have treated the matter as an exaggerated legend, but for my own part, I see no reason why it should not, in reality, be founded on fact. There is little doubt that the Asiatic poisoners were well acquainted with the infectious qualities of certain fevers and malignant diseases. Now, these very malignant diseases answer precisely to the description of a poison which has no immediate effects. Plant small-pox in the body of a man, and for a whole fortnight he walks about, well and hearty. Clothe a person with a garment soaked in typhus, and the same thing occurs—for many days there will be no sign of failure. Again, the gipsies, speaking a tongue which is essentially a deformed *prakrit*, and therefore Indian in origin, have long possessed a knowledge of the properties of the curious "*mucor phycomyces*." This was considered an algae by Agaron, but Mr. Berkeley refers it to the fungi. The gipsies are said to have administered the spores of this fungi in warm water. In this way they rapidly attach themselves to the mucous membrane of the throat, all the symptoms of a phthisis follow, and death takes place in from two to three weeks. Mr. Berkeley informs me that he has seen specimens growing on broth which had been rejected from the stomach, and that it develops in enormous quantities on oil casks and walls impregnated with grease. The filaments are long, from 12 to 18 inches, and it is capable of very rapid development.

There is also a modern poison, which, in certain doses, dooms the unfortunate individual to a terrible malady, simulating, to a considerable extent, natural disease; that is phosphorus. This poison was, however, unknown until some time in the eleventh century, when Alchid Becher, blindly experimenting on the distillation of urine and carbon, obtained his "*escar boucle*," and passed away without knowing the importance of his discovery, which, like so many others, had to be rediscovered at a later period.

The Hebrews were acquainted with certain poisons, the exact nature of which is not quite clear. The words "*rosch*" and "*chema*" seem to be used occasionally as a generic term for poison, and sometimes to mean a specific thing; "*rosch*," especially, is used to signify some poisonous parasitic plant. They knew yellow arsenic under the name of "*sam*," aconite under the name of "*boschka*," and possibly "*son*" means ergot.* In the later period of their history, when they were dispersed through various nations, they would naturally acquire the knowledge of those nations, without losing their own.

* R. J. Wunderbar, *Biblisch-talmudische Medicin*. Leipzig, 1850-60.

The part that poison has played in history is considerable. The pharmaceutical knowledge of the ancients is more graphically and terribly shown in the deaths of Socrates, Demosthenes, Hannibal and Cleopatra, than in the pages of the older writers on poisons.

In the reign of Artaxerxes II. (Mnemon), (B. C. 405-359), Phrysa poisoned the queen Statira by cutting food with a knife poisoned on one side only. Although this has been treated as an idle tale, yet two poisons, aconite and arsenic, were at least well known; either of these could have been in the way mentioned introduced in sufficient quantity into food to destroy life.

In the early part of the Christian era, professional poisoners arose, and for a long time exercised their trade with impunity. Poisoning was so much in use as a political engine that Agrippina (A.D. 26) refused to eat of some apples offered to her at table by her father-in-law, Tiberius.

It was at this time that the infamous Locusta flourished. She is said to have supplied, with suitable directions, the poison by which Agrippina got rid of Claudius; and the same woman was the principal agent in the preparation of the poison that was administered to Britannicus, by order of his brother Nero. The details of this interesting case have been recorded with some minuteness.

It was the custom of the Romans to drink hot water, a draught nauseous enough to us, but, from fashion or habit, considered by them a luxury; and, as no two men's tastes are alike, great skill was shown by the slaves in bringing the water to exactly that degree of heat which their respective masters found agreeable.*

The children of the Imperial house, with others of the great Roman families, sat at the banquets at a smaller side table, while their parents reclined at the larger. A slave brings hot water to Britannicus; it is too hot; Britannicus refuses it. The slave adds cold water; and it is this cold water that is supposed to have been poisoned; in any case, Britannicus had no sooner drunk of it than he lost voice and respiration. Agrippina, his mother, was struck with terror, as well as Octavia, his sister. Nero, the author of the crime, looks coldly on, saying that such fits often happened to him in infancy without evil result; and after a few moments' silence, the banquet goes on as before. If this were not sudden death from heart or brain disease, the poison must have been either a cyanide or prussic acid.

In those times no autopsy was possible; although the Alexandrian school, some 300 years before Christ, had dissected both the living and the dead, the work of Herophilus and Erasistratus had not been pursued, and the great Roman and Greek writers knew only the rudiments of

* Tacitus: lib. xii., xiii. Mentioned also by Juvenal and Suetonius.

human anatomy, while, as to pathological changes and their true interpretation, their knowledge may be said to have been absolutely *nil*. It was not, indeed, until the fifteenth century that the popes, silencing ancient scruples, authorized dissections; and it was not until the sixteenth century that Vesalius, the first worthy of being considered a great anatomist, arose. In default of pathological knowledge, the ancients attached great importance to mere outward marks and discolorations. They noted with special attention spots and lividity, and supposed that poisons singled out the heart for some quite peculiar action, altering its substance in such a manner that it resisted the action of the funeral pyre, and remained unconsumed. It may, then, fairly be presumed that many people must have died from poison without suspicion, and still more from the sudden effects of latent disease, ascribed wrongfully to poison. For example, the death of Alexander was generally at that time ascribed to poison; but Littré has fairly proved that the great emperor, debilitated by his drinking habits, caught a malarious fever in the marshes around Babylon, and died after eleven days' illness. If, added to sudden death, the body, from any cause, entered into rapid putrefaction, such signs were considered by the people absolutely conclusive of poisoning—this belief, indeed, prevailed up to the middle of the seventeenth century, and lingers still among the uneducated at the present day. Thus, when Britannicus died, an extraordinary lividity spread over the face of the corpse, which they attempted to conceal by painting the face. When Pope Alexander VI. died, probably enough from poison, his body, (according to Guicciardini) became a frightful spectacle—it was livid, bloated, and deformed; the gorged tongue entirely filled the mouth; from the nose flowed putrid pus, and the stench was horrible in the extreme.

All these effects of decomposition, we know, are apt to arise in coarse, obese bodies, and accompany both natural and unnatural deaths; indeed, if we look strictly at the matter, putting on one side the preservative effects of certain metallic poisons, it may be laid down that generally the corpses of those dying from poison are *less* apt to decompose rapidly than those dying from disease—this, for the simple reason that a majority of diseases cause changes in the fluids and tissues, which render putrefactive changes more active, while, as a rule, those who take poison are suddenly killed, with their fluids and tissues fairly healthy.

When the Duke of Burgundy desired to raise a report that John, Dauphin of France, was poisoned (1457), he described the imaginary event as follows:—

“One evening our most redoubtable lord and nephew fell so grievously sick that he died forthwith. His lips, tongue, and face were swollen; his eyes started out of his head. It was a horrible sight to see—for so look people that are poisoned.”

The favourite powder of the professional poisoner, arsenic, was known to crowned heads in the fourteenth century; and there has come down to us a curious document, drawn out by Charles le Mauvais, King of Navarre. It is a commission of murder, given to a certain Woudreton, to poison Charles VI., the Duke of Valois, brother of the king, and his uncles, the Dukes of Berry, Burgundy, and Bourbon:—

“ Go thou to Paris; thou canst do great service if thou wilt do what I tell thee; I will reward thee well. Thou shalt do thus: There is a thing which is called sublimed arsenic; if a man eat a bit the size of a pea, he will never survive. Thou wilt find it in Pampeluna, Bordeaux, Bayonne, and in all the good towns, through which thou wilt pass, at the apothecaries' shops. Take it, and powder it; and when thou shalt be in the house of the king, of the Count de Valois, his brother, the Dukes of Berry, Burgundy, and Bourbon, draw near, and betake thyself to the kitchen, to the larder, to the cellar, or any other place where thy point can be best gained, and put the powder in the soups, meats, or wines, provided that thou canst do it secretly. Otherwise, do it not.” Woudreton was detected, and executed in 1384.*

A chapter might be written, entitled “royal poisoners.” King Charles IX. even figures as an experimentalist.† An unfortunate cook has stolen two silver spoons, and, since there was a question whether “Bezoar” was an antidote or not, the king administers to the cook a lethal dose of corrosive sublimate, and follows it up with the antidote; but the man dies in seven hours, although Paré also gives him oil. Truly, a grim business!

The subtle method of removing troublesome subjects has been more often practised on the Continent than in England, yet the English throne in olden time is not quite free from this stain.‡ The use of

* *Trésor de Chartes.* Charles de Navarre. P. Mortonval, vol. ii., p. 384.

† *Oeuvres de Paré*, 2nd ed., liv. xx. *Des Vennes*, chap. xliv., p. 507.

‡ For example, King John is believed to have poisoned Maud Fitzwalter by “a poisoned egg.”

“ In the reign of King John, the White Tower received one of the first and fairest of a long line of female victims in that Maud Fitzwalter who was known to the singers of her time as Maud the Fair. The father of this beautiful girl was Robert, Lord Fitzwalter, of Castle Baynard, on the Thames, one of John's greatest barons. Yet the king, during a fit of violence with the queen, fell madly in love with this young girl. As neither the lady herself nor her powerful sire would listen to his disgraceful suit, the king is said to have seized her by force at Dunmow, and brought her to the Tower. Fitzwalter raised an outcry, on which the king sent troops into Castle Baynard and his other houses; and when the baron protested against these wrongs, his master banished him from the realm. Fitzwalter fled to France with his wife and his other children, leaving his daughter Maud in the Tower, where she suffered a daily insult in the

poison is wholly opposed to the Anglo-Saxon method of thought. To what anger the people were wrought on detecting poisoners, is seen in the fact that, in 1542, a young woman was boiled alive in Smithfield for poisoning three households.*

Two great criminal schools arose from the fifteenth to the seventeenth centuries in Venice and Italy. The Venetian poisoners are of earlier date than the Italian, and flourished chiefly in the fifteenth century. Here we have the strange spectacle, not of the depravity of individuals, but of the government of the state formally recognising secret assassination by poison, and proposals to remove this or that prince, duke, or emperor, as a routine part of their deliberations. Still more curious and unique, the dark communings of "*the council of ten*" were recorded in writing, and the number of those who voted for and who voted against the proposed crime, the reason for the assassination, and the sum to be paid, still exist in shameless black and white. Those who desire to study this branch of secret history may be referred to a small work by Carl Hoff, which gives a brief account of what is known of the proceedings of the council. One example will here suffice. On the 15th of December, 1513, a Franciscan brother, John of Ragubo, offered a selection of poisons, and declared himself ready to remove any objectionable person out of the way. For the first successful case he required a pension of 1500 ducats yearly, which was to be increased on the execution of future services. The presidents, Giro-lando Duoda and Pietro Guiarini, placed the matter before the "ten" on the 4th of January, 1514, and on a division (10 against 5) it was resolved to accept so patriotic an offer, and to experiment first on the Emperor Maximilian. The bond laid before the "ten" contained a regular tariff—for the great Sultan 500 ducats, for the King of Spain 150 ducats, but the journey and other expenses were in each case to be defrayed; the Duke of Milan was rated at 60, the Marquis of Mantua at 50, the pope could be removed at 100 ducats. The curious offer thus concludes: "The farther the journey, the more eminent the man, the

king's unlawful suit. On her proud and scornful answer to his passion being heard, John carried her up to the roof, and locked her in the round turret, standing on the northeast angle of the keep. Maud's cage was the highest, chilliest den in the Tower; but neither cold, nor solitude, nor hunger could break her strength. In the rage of his disappointed love, the king sent one of his minions to her room with a poisoned egg, of which the brave girl ate and died."—"Her Majesty's Tower." By Hepworth Dixon. Lond. 1869; i., p. 46.

* "This yeare, the 17th of March, was boyled in Smithfield one Margaret Davie, a mayden, which had pouysoned 3 householderes that she dwelled in. One being her mistress, which dyed of the same, and one Darington and his wyfe, which she also dwelled with in Coleman Street, which dyed of the same, and also one Tinleys, which dyed also of the same."—Wriothesley's "Chronicle," A.D. 1542.

more it is necessary to reward the toil and hardships undertaken, and the heavier must be the payment." The council appear to have quietly arranged thus to take away the lives of many public men, but their efforts were only in a few cases successful. When the deed was done, it was registered by a single marginal note, "*factum.*"

What drugs the Venetian poisoners used is uncertain. The Italians became notorious in the sixteenth and seventeenth centuries for their knowledge of poisons, partly from the deeds of Toffana and others, and partly from the works of J. Baptista Porta, who wrote a very comprehensive treatise under the title of "*Natural Magic*,"* and managed to slide into the text, in the sections on cooking (*De Re Coquinaria*, lib. xiv.) a mass of knowledge as to the preparation of poisons. There are prescriptions that little accord with the title, unless, indeed, the trades of cook and poisoner were the same. He gives a method of drugging wine with belladonna root, for the purpose of making the loaded guest loathe drink; he also gives a list of solanaceous plants, and makes special mention of *nux vomica*, aconite, veratrum, and mezereon. Again, in the section (*De Ancupio*, lib. xv.) he gives a recipe for a very strong poison, which he calls "*venenum lupinum*"; it is to be made of the powdered leaves of *Aconitum lycocitonum*, *Taxus baccata*, powdered glass, caustic lime, sulphide of arsenic, and bitter almonds, the whole to be mixed with honey, and made into pills the size of a hazel nut.

In the section *de Medicis Experimentis*, he gives a process to poison a sleeping person; the recipe is curious, and would certainly not have the intended effect. A mixture of hemlock juice, bruised datura, stramonium, belladonna, and opium is placed in a leaden box with a perfectly fitting cover, and fermented for several days; it is then opened under the nose of the sleeper. Possibly, Porta had experimented on small animals, and had found that such matters, when fermented, exhaled enough carbonic gas to kill them, and imagined, therefore, that the same thing would happen if applied to the human subject. However this may be, the account which Porta gives of the effects of the solanaceous plants, and the general tone of the work, amply prove that he was no theorist, but had studied practically the actions of poisons.

The iniquitous Toffana (or Tophana) made solutions of arsenious acid of varying strength, and sold these solutions in phials under the name of "*Acqua de Napoli*" for many years. She is supposed to have poisoned more than 600 persons, among whom were two popes—viz., Pius III. and Clement XIV. The composition of the Naples water was long a profound secret, but is said to have been known by the reigning pope and by the Emperor Charles VI. The latter told the secret to

* J. Bapt. Porta, born 1537. died 1615. *Neapolitani Magia Naturalis*. Neapoli, 1589.

Dr. Garelli, his physician, who, again, imparted the knowledge to the famous Friedrich Hoffman in a letter still extant. Toffana was brought to justice in 1709, but, availing herself of the immunity afforded by convents, escaped punishment, and continued to sell her wares for twenty years afterwards. When Kepfer* was in Italy he found her in a prison at Naples, and many people visited her as a sort of lion (1730). With the *Acqua Toffana*, the “*Acqetta di Perugia*” played at the same time its part. It is said to have been prepared by killing a hog, disjointing the same, strewing the pieces with white arsenic, which was well rubbed in, and then collecting the juice which dropped from the meat; this juice was considered far more poisonous than an ordinary solution of arsenic. The recent researches of Selmi on compounds containing arsenic, produced when animal bodies decompose in arsenical fluids, lend reason and support to this view; and probably the juice would not only be very poisonous, but act in a different manner, and exhibit symptoms different from those of ordinary arsenical poisoning. Toffana had disciples; she taught the art to Hieronyma Spara, who formed an association of young married women during the popedom of Alexander VII.; these were detected on their own confession.†

Contemporaneously with Toffana, another Italian, Keli, devoted himself to similar crimes. This man had expended much as an adept, searching for the philosopher’s stone, and sought to indemnify himself by entering upon what must have been a profitable business. He it was who instructed M. de St. Croix in the properties of arsenic, and St. Croix, in his turn, imparted the secret to his paramour, Madame de Brinvilliers. This woman appears to have been as cold-blooded as Toffana; she is said to have experimented on the patients at the Hôtel Dieu, in order to ascertain the strength of her powders, and to have invented “*les poudres de succession*.” She poisoned her father, brothers, sister, and others of her family; but a terrible fate overtook both her and St. Croix. The latter was suffocated by some poisonous matters he was preparing, and Madame de Brinvilliers’ practices having become known, she was obliged to take refuge in a convent. Here she was courted by a police officer disguised as an abbé, lured out of the convent, and, in this way, brought to justice, was beheaded and burned near Nôtre Dame in the middle of the reign of Louis XIV.‡

* Kepfer’s “Travels.” Lond. 1758.

† Le Bret’s *Magazin zu Gebräuche der Staat-u. Kirchen-Geschichte*, Theil 4. Frankfort and Leipzig, 1774.

‡ For the court of poisoners (*chambre ardente*) and the histories of St. Croix De Brinvilliers, the priest Le Sage, the women La Voisin and La Vigoureux, the reader may be referred to Voltaire’s *Siècle de Louis XIV.*, Madame de Sévigné’s *Lettres*, Martiniére’s *Hist. de la Règne de Louis XIV.*, Strutzel, *De Venenis*, &c.

The numerous attempts of the Italian and Venetian poisoners on the lives of monarchs and eminent persons, cast for a long time a cloud over regal domestic peace. Bullets and daggers were not feared, but in their place the dish of meat, the savoury pastry, and the red wine were regarded as possible carriers of death. No better example of this dread can be found than, at so late a period as the reign of Henry VIII.* the extraordinary precautions thought necessary for preserving the infant Prince of Wales.

"No person of whatsoever rank, except the regular attendants in the nursery, should approach the cradle, except with an order from the king's hand. The food supplied to the child was to be largely '*assayed*,' his clothes were to be washed by his own servants, and no other hand might touch them. The material was to be submitted to all tests. The chamberlain and vice-chamberlain must be present, morning and evening, when the prince was washed and dressed, and nothing of any kind, bought for the use of the nursery, might be introduced until it was washed and perfumed. No person, not even the domestics of the palace, might have access to the prince's rooms, except those who were specially appointed to them, nor might any member of the household approach London, for fear of their catching and conveying infection.†"

However brief and imperfect the foregoing historical sketch of the part that poison has played may be, it is useful in showing the absolute necessity of toxicological science—a science embracing many branches of knowledge. If it is impossible for Toffanas, Locustas, and other specimens of a depraved humanity, to carry on now their crimes without detection; if poison is the very last form of death feared by eminent political persons: it is not so much owing to a different state of society, as to the more exact scientific knowledge which is applied during life to the discrimination of symptoms, distinguishing between those resulting from disease and those due to injurious substances, and after death to a highly-developed pathology, which has learned, by multiplied observations, all the normal and abnormal signs in tissues and organs; and, finally, to an ever-advancing chemistry, which is able in many instances to separate and detect the hurtful and noxious thing, although hid for months deep in the ground.

* Henry VIII., at one time of his life, was (or pretended to be) apprehensive of being poisoned; it was, indeed, a common belief of his court that Anne Boleyn attempted to dose him. "The king, in an interview with young Prince Henry, burst into tears, saying that he and his sister (meaning the Princess Mary) might thank God for having escaped from the hands of that accursed and venomous harlot, who had intended to poison them."—"A Chronicle of England during the Reign of the Tudors." By W. J. Hamilton. Introduction p. xxi.

† Froude's "History of England," vol. iii., p. 262.

II.—GROWTH AND DEVELOPMENT OF THE MODERN METHODS OF CHEMICALLY DETECTING POISONS.

The history of the detection of poisons has gone through several phases. The first phase has already been incidentally touched upon—*i.e.*, detection by antecedent and surrounding circumstances, aided sometimes by experiments on animals. If the death was sudden, if the *post-mortem* decomposition was rapid, poison was indicated—sometimes a portion of the food last eaten, or the suspected thing, would be given to an animal; if the animal also died, such accumulation of proof would render the matter beyond doubt. The modern toxicologists are more sceptical, for even the last test is not of itself satisfactory. It is now known that meat may become filled with bacilli, and produce rapid death, and yet no poison as such has been added.*

In the next phase, the doctors were permitted to dissect, and to familiarise themselves with pathological appearances. This was a great step gained; the apoplexies, heart diseases, perforations of the stomach, and fatal internal haemorrhages could no longer be ascribed to poison. If popular clamour made a false accusation, there was more chance of a correct judgment. It was not until the end of the eighteenth and the beginning of the present century, however, that chemistry was far enough advanced to test for the more common mineral poisons; the modern phase was then entered on, and toxicology took a new departure.

From the treatise of Barthélémy d'Anglais † in the thirteenth century (in which he noticed the poisonous properties of quicksilver vapour), up to the end of the fifteenth century, there are numerous treatises upon poison, most of which are mere learned compilations, and scarcely repay perusal.

In the sixteenth century there are a few works, such, for example, as that of Porta, which partook of the general advancement of science, and left behind the stereotyped doctrine of the old classical schools.‡

In the seventeenth century, the Honorable Robert Boyle made some shrewd observations, bearing on toxicology, in his work on “The Usefulness of Natural Philosophy,” &c.; Oxford, 1664. Nicolas

* “Appendix to the Medical Officers’ Report to the Local Government Board for 1880.”

† *De Rerum Proprietaribus.*

‡ In the sixteenth century, it was not considered proper to write upon poisons. Jerome Cardan declared a poisoner worse than a brigand, “and that is why I have refused not only to teach or experiment on such things, but even to know them.” —*J. Cardan: De Subtilitate.* Basel, 1558.

L'Emery also wrote a *Cours de Chimie*,—quite an epitome of the chemical science of the time.*

In the eighteenth century, still further advances were made. Richard Mead published his ingenious “Mechanical Theory of Poisons.” Great chemists arose—Stahl, Marggraf, Brandt, Bergmann, Scheele, Berthollet, Priestley, and lastly, Lavoisier—and chemistry, as a science, was born. Of the chemists quoted Scheele, in relation to toxicology, stands chief. It was Scheele who discovered prussic acid,† without however, noting its poisonous properties; and the same chemist separated oxalic acid from sorrel,‡ made the important discovery that arsenic united with hydrogen, forming a foetid gas, and, moreover, that this gas could be decomposed by heat.§ From this observation, a delicate test for arsenic was afterwards elaborated, which, for the first time, rendered the most tasteless and easily administered poison in the whole world at once the easiest of detection. The further history of what is now called “Marsh’s Test” is as follows:—

Proust ¶ observed that a very foetid hydrogen gas was disengaged when arsenical tin was dissolved in hydrochloric acid, and that arsenic was deposited from the inflamed gas on cold surfaces, which the flame touched. Trommsdorff next announced, in 1803, that when arsenical zinc was introduced into an ordinary flask with water and sulphuric acid, an arsenical hydrogen was disengaged, and if the tube was sufficiently long, arsenic was deposited on its walls.¶ Stromeyer, Gay-Lussac, Thenard, Gehlen, and Davy, later, studied the gas, and Serullas, in 1821, proposed this reaction as a toxicological test. Lastly, in 1836, Marsh published his “Memoir.”** He elaborated a special apparatus of great simplicity, developed hydrogen by means of zinc and sulphuric acid, inflamed the issuing gas, and obtained any arsenic present as a metal, which could be afterwards converted into arsenious acid, &c.

This brief history of the so-called “Marsh’s Test” amply shows

* *Cours de Chimie, contenant la manière de faire les opérations qui sont en usage dans la Médecine.* Paris, 1875.

† *Opuscula Chemica*, vol. ii., pp. 148-174.

‡ *De Terra Rhubarbi et Acido Acetosellæ. Nova Acta Acad. Veg. Sued. Anni 1784. Opuscula Chemica*, vol. ii., pp. 187-195.

Bergmann first described oxalic acid as obtained by the oxidation of saccharine bodies; but Scheele recognised its identity with the acid contained in sorrel.

§ *Mémoires de Scheele*, t. i., 1775.

¶ *Proust, Annales de Chimie*, t. xxviii., 1798.

¶ Nicholson’s “Journal,” vol. vi.

** “Description of a New Process of Separating Small Quantities of Arsenic from substances with which it is Mixed.” Ed. *New Phil. Journal*, 1836.

that Marsh was not the discoverer of the test. Like many other useful processes, it seems to have been evolved by a combination of many minds. It may, however, be truly said that Marsh was the first who perfected the test, and brought it prominently forward.

Matthieu Joseph Bonaventura Orfila must be considered the father of modern toxicology. His great work, *Traité de Toxicologie*, was first published in 1814, and went through many editions. Orfila's chief merit was the discovery that poisons were absorbed and accumulated in certain tissues—a discovery which bore immediate fruit, and greatly extended the means of seeking poisons. Before the time of Orfila, a chemist not finding anything in the stomach would not have troubled to have examined the liver, the kidney, the brain, or the blood. The immense number of experiments which Orfila undertook is simply marvellous. Some are of little value, and teach nothing accurately as to the action of poisons—as, for example, many of those in which he tied the gullet in order to prevent vomiting, for such are experiments under entirely unnatural conditions ; but there are still a large number which form the very basis of our pathological knowledge.

Orfila's method of experiment was usually to take weighed or measured quantities of poison, to administer them to animals, and then after death—first carefully noting the changes in the tissues and organs—to attempt to recover by chemical means the poison administered. In this way he detected and recovered nearly all the organic and inorganic poisons then known, and most of his processes are, with modifications and improvements, in use at the present time.*

The discovery of the alkaloids at the commencement of this century certainly gave the poisoner new weapons ; yet the same processes (slightly modified) which separated the alkaloids from plants, also served to separate them from the human body. In 1803, Derosne discovered narcotine and morphine, but he neither recognised the difference between these two substances, nor their basic properties. Sertürner from 1805 devoted himself to the study of opium, and made a series of discoveries. Robiquet, in 1807, recognised the basic characters of narcotine. In 1818, Pelletier and Caventou separated strychnine ; in 1819, brucine, and in the same year delphinine was discovered simultaneously by Brande, Lassaigne, and Feneuille. Coniine was recognised by Giesecke

* Orfila's chief works are as follows:—

Traité de Toxicologie. 2 vols. 8vo. Paris, 1814.

Leçons de Chimie, appliquées à la Méd. Pratique, 16mo. Brussels, 1836.

Mémoire sur la Nicotine et la Conicine. Paris, 1851.

Leçons de la Méd. Légale. 8vo. Paris, 1821.

Traité des Exhumations Juridiques, et Considérations sur les Changemens Physiques que les Cadavres éprouvent en se pourrisant. 2 tom. Paris, 1831.

in 1827, and in the following year, 1828, nicotine was separated by Reimann and Posselt. In 1832, Robiquet discovered codeine; and in 1833, atropine, aconitine, and hyoscyamine were distinguished by Geiger and Hesse. Since then, every year has been marked by the separation of some new alkaloid from either animal or vegetable substances. So many workers in different countries now began to study and improve toxicology, that it would exceed the limits, and be foreign to the scope of this treatise, to give even a brief *résumé* of their labours. It may, notwithstanding, be useful to append a short bibliography of the chief works on toxicology of the present century.

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PART II.

I. DEFINITION OF POISON.

The term "*Poison*" may be considered first in its legal, as distinct from its scientific, aspect.

The legal definition of "poison" is to be gathered from the various statute-books of civilised nations.

The English law enacts that: "Whoever shall administer, or cause to be administered to, or taken by any person, any poison or other destructive thing, with intent to commit murder, shall be guilty of felony."

Further, by the Criminal Consolidation Act, 1861: "Whosoever shall, by any other means other than those specified in any of the preceding sections of this Act, attempt to commit murder, shall be guilty of felony."

It is therefore evident that, by implication, the English law defines a poison to be a destructive thing administered to, or taken by, a person, and it must necessarily include, not only poisons which act on account of their inherent chemical and other properties after absorption into the blood, but mechanical irritants, and also specifically-tainted fluids. Should, for example, a person give to another milk, or other fluid, knowing, at the same time, that such fluid is contaminated by the specific poison of scarlet fever, typhoid, or any serious malady capable of being thus conveyed, I believe that such an offence could be brought under the first of the sections quoted. In fine, the words "*destructive thing*" are widely applicable, and may be extended to any substance, gaseous, liquid, or solid, living or dead, which, if capable at all of being taken within the body, may injure or destroy life. According to this view, the legal idea of "*poison*" would include such matters as boiling water, molten lead, specifically-infected fluids, the flesh of animals dying of diseases which may be communicable to man, powdered glass, diamond dust, &c. Evidence must, however, be given of guilty intent.

The words, "administered to or taken by," imply obviously that the framers of the older statute considered the mouth as the only portal of entrance for criminal poisoning, but the present law effectually guards against any attempt to commit murder, no matter by what means. There is thus ample provision for all the strange ways by which poison has been introduced into the system, whether it be by the ear, nose, brain, rectum, vagina, or any other conceivable way, so that (to

borrow the words of Mr. Greaves, "Notes on Criminal Law Consolidation") "the malicious may rest satisfied that every attempt to murder which their perverted ingenuity may devise, or their fiendish malignity suggest, will fall within some clause of this Act, and may be visited with penal servitude for life."

Since poison is often exhibited, not for the purpose of taking life, but from various motives, and to accomplish various ends—as, for example, to narcotise the robber's victim (this especially in the East), to quiet children, to create love in the opposite sex (love philters), to detect the secret sipper by suitably preparing the wine, to expel the inconvenient fruit of illicit affection, to cure ineptitude by polluting the drunkard's drink with antimony, and, finally, to satisfy an aimless spirit of mere wantonness and wickedness, the English law enacts "that whosoever shall unlawfully or maliciously administer to, or cause to be taken by, any other person, any poison or other destructive or noxious thing, so as thereby to endanger the life of such person, or so as thereby to inflict upon such person any grievous bodily harm, shall be guilty of felony."

There is also a special provision, framed evidently, with reference to volatile and stupefying poisons, such as chloroform, tetrachloride of carbon, &c.:—

"Whoever shall unlawfully apply, or administer to, or cause to be taken by any person, any chloroform, laudanum, or other stupefying or overpowering drug, matter, or thing, with intent, in any such case, thereby to enable himself or any other person to commit, or with intent, &c., to assist any other person in committing, any indictable offence, shall be guilty of felony."

The German statute, as with successive amendments it now stands, enacts as follow:—*

"Whoever wilfully administers (*beibringt*) to a person, for the purpose of injuring health, poison, or any other substance having the

* "Wer vorsätzlich einem Anderen, um dessen Gesundheit zu beschädigen, Gift oder andere Stoffe, beibringt, welche die Gesundheit zu zerstören geeignet sind, wird mit Zuchthaus von zwei bis zu zehn Jahren bestraft.

"Ist durch die Handlung eine schwere Körperverletzung verursacht worden, so ist auf Zuchthaus nicht unter fünf Jahren, und wenn durch die Handlung der Tod verursacht worden, auf Zuchthaus nicht unter zehn Jahren oder auf lebenslängliches Zuchthaus zu erkennen.

"Ist die vorsätzliche rechtswidrige Handlung des Gift—&c.—Bebringens auf das 'Tödten' gerichtet, soll also durch dieselbe gewollter Weise der Tod eines Anderen herbeigeführt werden, so kommt in betracht: Wer vorsätzlich einen Menschen tötet, wird, wenn er die Tötung mit Ueberlegung ausgeführt hat, wegen Mordes mit dem Tode bestraft."

property of injuring health, will be punished by from two to ten years' imprisonment.

"If by such act a serious bodily injury is caused, the imprisonment is not to be less than five years; if death is the result, the imprisonment is to be not under ten years or for life.

"If the death is wilfully caused by poison, it comes under the general law: 'Whoever wilfully kills a man, and, if the killing is pre-meditated, is on account of murder punishable with death.'"

The French law runs thus (Art. 301, *Penal Code*):—"Every attempt on the life of a person, by the effect of substances which may cause death, more or less suddenly, in whatever manner these substances may have been employed or administered, and whatever may have been the results, is called poisoning."*

There is also a penalty provided against any one who "shall have occasioned the illness or incapacity for personal work of another, by the voluntary administration, in any manner whatever, of substances which, without being of a nature to cause death, are injurious to health."†

Scientific Definition of a Poison.—A true scientific definition of a poison must exclude all those substances which act mechanically,—the physical influences of heat, light, and electricity; the various infections which are supposed to be associated with and caused by the growth and multiplication of minute organisms; and further, the true parasitic diseases, whether caused by the growth of fungus, or the invasion of an organism by animal parasites, as, for example, "trichinosis." The definition of poison, in a scientific sense, should be broad enough to comprehend not only the human race, but the dual world of life, both animal and vegetable.

Husemann is almost the only writer on poisons who has attempted, with more or less success, to define poison by a generalisation, keeping in view the exclusion of the matters enumerated. Husemann says—
"We define poisons, as such inorganic, or organic, substances as are in part capable of artificial preparation; in part existing, ready-formed, in the animal or vegetable kingdom, which, without being able to reproduce themselves, through the chemical nature of their molecules under certain conditions, change in the healthy organism the form and general relation-

* *Est qualifié empoisonnement*—tout attentat à la vie d'une personne par l'effet de substances qui peuvent donner la mort plus ou moins promptement, de quelque manière que ces substances aient été employées ou administrée, et quelles qu'en aient été les suites."—Art. 301, *Penal Code*.

† "Celui qui aura occasionné à autrui une maladie ou incapacité de travail personnel en lui administrant volontairement, de quelque manière que ce soit, des substances qui, sans être de nature à donner la mort, sont nuisibles à la santé."—Art. 317, *Penal Code*.

ship of the organic parts, and through annihilation of organs, or destruction of their functions, injure health, or, under certain conditions, destroy life."

I would make an attempt to define a poison thus:—*A substance of definite chemical composition, whether mineral or organic, may be called a poison, if it is capable of being taken into any living organism, and causes, by its own inherent chemical nature, impairment or destruction of function.*

It will, I think, be admitted that all poisons hitherto discovered have definite chemical compositions, and can be represented by definite chemical formulæ; and if in every case the active principle of certain poisonous secretions has not yet been separated in either a pure enough state or in sufficient quantity to admit of analysis and determination of the nature of the chemical molecules, it is none the less certain that the venoms of all the snakes, the poison of the stinging insects, and the more complicated vegetable juices contain either one active principle, or a mixture of several, which, in the progress of chemistry, will eventually be separated. Not so the various bacteroid-like bodies which have been discovered in anthrax, small-pox, tuberclosis, diphtheria, &c. Here there is no probability that—supposing they could be purified perfectly from the medium in which they live, and submitted to analysis—any formula could be constructed of a satisfactory character, or any active principle be separated by chemical means which would reproduce the effects observable in their action on animal life.

II.—CLASSIFICATION OF POISONS.

At some future time, with a more intimate knowledge of the way in which each poison acts upon the various forms of animal and vegetable life, it may be possible to give a truly scientific and philosophical classification of poisons—one based neither upon symptoms, upon local effects, nor upon chemical structure, but upon a collation and comparison of all the properties of a poison, whether chemical, physical, or physiological. The general arrangement of nearly all toxicologists has hitherto been based upon the physiological effects of poisons.

Fodéré divided poisons into narcotics, narcotico-acrids, and septics. Orfila into—

I. CORROSIVES:—

1. Mineral corrosive.
2. Vegetable corrosive.
3. Animal corrosive poisons.

II. NARCOTIC.

III. IRRITANT NARCOTIC.

IV. SEPTIC.

Casper, in the earlier editions of his handbook, adopted a physiological arrangement, but afterwards omitted all classification.

Taylor's division was as follows :—

I. IRRITANT POISONS :—

1. Mineral irritants.
2. Vegetable and animal irritants.

II. NEUROTIC POISONS :—

1. General or narcotic poisons.
2. Spinal poisons.
3. Cerebro-spinal poisons.

III. POISONOUS GASES :—

1. Irritant-poisonous gases.
2. Neurotic-poisonous gases.

Dr. Guy adopted a partly chemical and partly physiological arrangement thus :—

I. INORGANIC :—

- a. Corrosive.
- b. Irritant.

II. ORGANIC :—

- a. Irritant.
- b. Affecting the brain
- c. ,, ,, spinal cord.
- d. ,, ,, heart.
- e. ,, ,, lungs.

These authors themselves would be the first to admit the imperfection of their various classifications ; and therefore, as it is universally acknowledged, that no perfect systematic arrangement is at present attainable, we are either compelled to omit all classification, or else to arrange poisons with a view to practical utility merely,

From the latter point of view, an arrangement simply according to the most prominent symptoms is a good one, and, without doubt, an assistance to the medical man summoned in haste to a case of real or suspected poisoning. Indeed, under such circumstances, a scheme somewhat similar to the following, probably occurs to every one versed in toxicology :—

A. POISONS CAUSING DEATH IMMEDIATELY, OR IN A FEW MINUTES.

There are but few poisons which destroy life in a few minutes. Omitting the strong mineral acids and carbonic anhydride, with the irrespirable gases—*Prussic acid, the cyanides, oxalic acid*, and, occasionally, *strychnine*, are the chief poisons coming under this head.

B. IRRITANT POISONS (symptoms mainly pain, vomiting, and purging).

Arsenic, antimony, phosphorus, cantharides, savin, ergot, digitalis, colchicum, zinc, mercury, lead, copper, silver, iron, baryta, chrome, yew, laburnum, and putrid animal substances.

C. IRRITANT AND NARCOTIC POISONS (symptoms those of an irritant nature, with the addition of more or less pronounced cerebral indications).

To this class more especially belong *oxalic acid*, and *the oxalates*, with several poisons belonging to the purely narcotic class, but which produce occasionally irritant effects.

D. POISONS MORE ESPECIALLY AFFECTING THE NERVOUS SYSTEM.

1. NARCOTICS (chief symptom insensibility, which may be preceded by more or less cerebral excitement) : *Opium, chloral, chloroform.*

2. DELIRIANTS (delirium for the most part a prominent symptom) : *Belladonna, hyoscyamus, stramonium, with others of the Solanaceæ*, to which may be added—*poisonous fungi, Indian hemp, lolium temulentum, aenanthe crocata, and camphor.*

3. CONVULSIVES.—Almost every poison has been known to produce convulsive effects, but the only true convulsive poisons are the *alkaloids of the strychnos class.*

4. COMPLEX NERVOUS PHENOMENA : *Aconite, digitalis, hemlock, calabar bean, tobacco, lobelia inflata and curara.*

However useful this “rough and ready” list of poisons, classed according to their effects, may be to the practitioner, I have preferred an arrangement which, as far as possible, follows the order in which a chemical expert would search for an unknown poison—hence an arrangement partly chemical and partly symptomatic. A chemist, given a liquid to examine, would naturally test first its reaction, and, if strongly alkaline or strongly acid, would at once direct his attention to the mineral acids or to the alkalies. In other cases, he would proceed to separate volatile matters from those that were fixed, lest substances such as prussic acid, chloroform, alcohol, and phosphorus be dissipated or destroyed by his subsequent operations.

Distillation over, the alkaloids, glucosides, and their allies would next be naturally sought, since they can be extracted by alcoholic and ethereal solvents in such a manner as in no way to interfere with an *after-search* for metals.

The metals are last in the list, because, by suitable treatment, after all organic substances are destroyed, either by actual fire or powerful chemical agencies, even the volatile metals may be recovered. The metals are arranged very nearly in the same order as that in which they would be separated from a solution—viz., according to their behaviour to hydric and ammonic sulphides.

There are a few poisons, of course, such as the oxalates of the alkalies, which might be overlooked, unless sought for specially; but it is hoped that this is no valid objection to the arrangement suggested, which, in greater detail, is as follows:—

A.—ACIDS AND ALKALIES.

1. Sulphuric acid.
2. Hydrochloric acid.
3. Nitric acid.
4. Potash.
5. Soda.
6. Ammonia.
7. Neutral, sodium, potassium, and ammonium salts.

In nearly all cases of death from any of the above, the analyst from the symptoms observed during life, from the surrounding circumstances, and from the pathological appearances and evident chemical reactions of the fluids submitted, is put at once on the right track, and has no difficulty in obtaining decided results.

B.—POISONOUS SUBSTANCES CAPABLE OF BEING SEPARATED BY DISTILLATION FROM EITHER NEUTRAL OR ACID LIQUIDS.

1. Hydrocarbons.
2. Camphor.
3. Alcohols.
4. Amyl-nitrite.
5. Chloroform and other anæsthetics.
6. Carbon disulphide.
7. Carbolic acid.
8. Nitro-benzene.
9. Prussic-acid.
10. Phosphorus.

I have not thought well to include in this class the volatile alkaloids, which may also be readily distilled by strongly alkalising the fluid, because they admit of a rather different mode of treatment.

C.—ALKALOIDS AND POISONOUS VEGETABLE PRINCIPLES SEPARATED FOR THE MOST PART BY ALCOHOLIC SOLVENTS.

DIVISION I.—VEGETABLE ALKALOIDS.

1. General methods of testing and extracting alkaloids.
2. Liquid volatile alkaloids, alkaloids of hemlock, nicotine, piturie, sparteine.
3. The opium group of alkaloids.
4. The strychnine or tetanic group of alkaloids—strychnine, brucine, igasurine.
5. The aconite group of alkaloids.
6. The mydriatic group of alkaloids—atropine, hyoscyamine, solanine, cytisine.
7. The alkaloids of the veratrines.
8. Physostigmine.
9. Pilocarpine.
10. Taxine.
11. Curarine.
12. Colchicine.
13. Muscarine and the active principles of certain fungi.

There would, perhaps, have been an advantage in arranging several of the individual members somewhat differently—*e. g.*, a group might be made of poisons, which, like pilocarpine and muscarine, are antagonistic to atropine; and another group suggests itself, the physiological action of which is the opposite of the strychnos class; solanine (although classed as a mydriatic, and put near to atropine), has much of the nature of a glucoside, and the same may be said of colchicine; so that, if the classification were made solely on chemical grounds, solanine would have followed colchicine, and thus have marked the transition from the alkaloids to the glucosides.

DIVISION II.—GLUCOSIDES.

1. The digitalis group.
2. Other poisonous glucosides acting on the heart.
3. Saponin.

The glucosides, when fairly pure, are easily recognised; they are destitute of nitrogen, neutral in reaction, and split up into sugar, and other compounds when submitted to the action of saponifying agents, such as boiling with dilute mineral acids.

DIVISION III.—CERTAIN POISONOUS ANHYDRIDES OF THE ORGANIC ACIDS.

1. Santonin.

2. Mezerein.

It is probable that this class will in a few years be extended, for several other organic anitrogenous poisons exist, which, when better known, will most likely prove to be anhydrides.

DIVISION IV.—VARIOUS VEGETABLE POISONOUS PRINCIPLES NOT ADMITTING OF CLASSIFICATION UNDER THE PREVIOUS THREE DIVISIONS.

Ergot, picrotoxin, the poison of *Illicium religiosum*, cicutoxin, *Aethusa cynapium*, *Cenanthus crocata*, croton oil, savin oil.

The above division groups together various miscellaneous toxic principles, none of which can at present be satisfactorily classified.

D.—POISONS DERIVED FROM LIVING OR DEAD ANIMAL SUBSTANCES.

DIVISION I.—POISONS SECRETED BY THE LIVING.

1. Poisonous amphibia.
2. Poison of the scorpion.
3. Poisonous fish.
4. Poisonous insects—spiders, wasps, bees, beetles, &c.
5. Snake poison.

DIVISION II.—POISONS FORMED IN DEAD ANIMAL MATTERS.

1. Ptomaines.
2. Poisoning by putrid or changed foods—sausage poisoning.

E.—THE OXALIC ACID GROUP.

F.—INORGANIC POISONS.

DIVISION I.—PRECIPITATED FROM A HYDROCHLORIC ACID SOLUTION BY HYDRIC SULPHIDE—PRECIPITATE, YELLOW OR ORANGE.

Arsenic, antimony, cadmium.

DIVISION II.—PRECIPITATED BY HYDRIC SULPHIDE IN HYDROCHLORIC ACID SOLUTION—BLACK.

Lead, copper, bismuth, silver, mercury.

DIVISION III.—PRECIPITATED FROM A NEUTRAL SOLUTION BY HYDRIC SULPHIDE.

Zinc, nickel, cobalt.

DIVISION IV.—PRECIPITATED BY AMMONIC SULPHIDE.

Iron, chromium, thallium.

DIVISION V.—ALKALINE EARTHS.

Barium.

APPENDIX.—Examination of Blood and of Blood Spots.

III.—STATISTICS.

The number of deaths from poison (whether accidental, suicidal, or homicidal), as compared with other forms of violent, as well as natural deaths, possesses no small interest; and this is more especially true when the statistics are studied in a comparative manner, and town be compared with town, country with country.

The greater the development of commercial industries (especially those necessitating the use or manufacture of powerful chemical agencies), the more likely are accidents from poison to occur. It may also be stated, further, that the higher the mental development of a nation, the more likely are its homicides to be caused by subtle poison—its suicides by the euthanasia of chloral, morphine, or hemlock.

Other influences causing local diversity in the kind and frequency of poisoning, are those of race, of religion, of age and sex, and the mental stress concomitant with sudden political and social changes.

In the five years from 1863–1867, there appear to have died from poison, in England and Wales, 2097 persons. In a certain number (1,620) of these cases, the poison, with more or less clearness, is indicated, and the causes of death may be arranged in the order of frequency, thus:

TABLE I.—DEATHS FROM POISON BETWEEN 1863–1867

Opiates,	{ Opium and Laudanum,	426	
	Opium,	114	{
	Morphia,	32	
	Godfrey's Cordial,	56	
Lead Salts,			242
Cyanides,	{ Cyanide of Potash and Prussic Acid,	151	{
	Oil of Bitter Almonds,	31	
Arsenic,			83
Acids,	{ Sulphuric Acid,	53	{
	Nitric Acid,	16	
	Hydrochloric Acid,	5	
Oxalic Acid,			66
Mercury,			58
Strychnine,			41
Alcohol,			35
Worm Powder,			20
Phosphorus,			15
Ammonia and Hartshorn,			11

TABLE I.—DEATHS FROM POISON BETWEEN 1868-1867—Continued.

Throwing out the 110 cases which cannot be accurately defined, it would then seem likely that, in the years mentioned, a thousand cases of poisoning—accidental, homicidal, and suicidal—would be arranged thus:—

Opiates,	414
Lead Salts,	159
Cyanides,	113
Arsenic,	55
Oxalic Acid,	43
Mineral Acids,	42
Mercury,	33
Strychnine,	27
Alcohol,	23
Phosphorus,	9

The remaining 82 would be of a miscellaneous character.

TABLE II.*—SUBSTANCES EMPLOYED IN 1000 MALE AND FEMALE SUICIDES BY POISON IN ENGLAND DURING THE TEN YEARS, 1871-1880.

Poison.	Males.	Females.	Total
OPIATES,	256.5	167.1	423.6
CYANIDES—			
Prussic Acid, Oil of Almonds,	178.4	27.5	
Cyanide of Potassium,	111.1	89.6	356.6
Vermin-Killer, and Fly-Killer,	47.6	194.5	242.1
Carbolic Acid,	57.4	180.9	188.3
Strychnine,	79.4	108.8	182.7
MINERAL ACIDS—			
Acid Hydrochloric	39.1	84.5	
" Sulphuric,	22.0	39.6	170.2
" Nitric..	19.5	15.5	
Oxalic Acid, Salts of Sorrel,	70.8	87.8	158.6
Arsenic,	28.1	51.6	79.7
Mercury,	23.2	27.5	50.7
Phosphorus,	11.0	24.1	35.1
Chloroform, Chloral, and Chlorodyne,	15.9	8.6	24.5
Ammonia,	11.0	8.6	19.6
Belladonna,	6.1	8.6	14.7
Aconite,	6.1	8.4	9.5
Copper,	1.2	6.9	8.1
Benzoline, Parrafin,	4.8	1.7	6.5
Chloride of Zinc, Disinfecting Fluid,	2.4	8.4	5.8
Lead,	1.2	8.4	4.6
Liniment,		8.4	8.4
Bichromate of Potash,	1.2	1.7	2.9
Alcohol,	1.7	1.7
Colocynth,	1.7	1.7
Hellebore,	1.7	1.7
Iodine,	1.7	1.7
Acetic Acid,	1.2	...	1.2
Cantharides,	1.2	...	1.2
Colchicum,	1.2	...	1.2
Tartaric Acid,	1.2	...	1.2
Yew,	1.2	...	1.2

* The total deaths from poison in the five years ending 1880 in England, were 1581, and may be classified as follows:—

	Accident or Negligence.		Suicide.		Murder.	
	M.	F.	M.	F.	M.	F.
1876,	37	31	36	23	1	2
1877,	49	24	24	20	1	0
1878,	234	116	116	99	1	2
1879,	229	139	143	104	0	4
1880,	48	20	52	21	1	0
	507	330	373	267	4	8

It is useful to compare the two previous tables together. The second list, as might be expected, is at once more definite and more complete. Opiates hold the first place in both, but the extended use of carbolic acid has introduced a new and ever ready means of suicide. The mineral acids, as before, occupy the sixth place, but arsenic does not appear to be such a favoured medium of suicide as in former years.

TABLE III.—SHOWING THE ADMISSIONS INTO VARIOUS MEDICAL INSTITUTIONS* IN BERLIN OF PERSONS SUFFERING FROM THE EFFECTS OF POISON DURING THE THREE YEARS, 1876, 1877, 1878.

		Males.	Females.	Total.
Charcoal Vapour,	.	77	8	155
Sulphuric Acid,	.	24	4	
Hydrochloric Acid,	.	4	4	93
Nitric Acid, and Aqua Regia,	.	7	.	
Phosphorus,	.	13	8	41
Cyanide of Potash,	.	29	3	
Prussic Acid,	.	5	1	38
Oxalic Acid, and Oxalate of Potash,	.	11	8	19
Alcohol,	.	12	2	14
Arsenic,	.	7	5	
Morphine,	.	8	1	12
Opium,	.	2	1	
Potash or Soda Lye,	.	2	6	8
Chloral,	.	3	4	
Chloroform,	.	4	2	6
Sewer Gas,	.	5	.	5
Strychnine,	.	.	4	4
Atropine,	.	1	2	
Copper Sulphate,	.	1	2	3
Nitrobenzol,	.	2	.	2
Carbolic Acid,	.	.	2	2
Chromic Acid,	.	1	1	
Burnt Alum,	.	.	1	1
Ammonium Sulphide,	.	1	.	1
Datura Stramonium,	.	.	1	1
Petroleum,	.	.	1	1
Benzine,	.	1	.	1
Ether,	.	1	.	1
Prussic Acid and Morphine,	.	1	.	1
Prussic Acid and Chloral,	.	1	.	1
Turpentine and Sal Ammoniac,	.	..	1	1
		223	212	435

* Viz., the Königl. Charité Alig. Städtisches Krankenhaus, Städtisches Bar-acken-Lazsreth, Bethanien. St. Helwög's-Mazarus, Elisabethen-Krankenhaus Augusta Hospital, and the Institut für Staatsarzneikunde.

The probability, then, is strong that 1000 deaths from poison in or about Berlin would be made up as follows:—

Charcoal Vapour,	356
Mineral Acids,	214
Phosphorus,	94
Cyanides— <i>i.e.</i> , Potassic Cyanide and Prussic Acid,	90
Oxalic Acid and Oxalates,	44
Alcohol,	32
Opium and Morphia,	28
Arsenic,	28
Chloral,	16
Chloroform,	14
Sewer Gas,	11
Strychnine,	9
Atropine,	7
Sulphate of Copper,	7
Nitro-Benzol,	5
Carbolic Acid,	5
Chromic Acid,	5

The remaining thirty-five will be made up of the more uncommon poisonings, either of matters but little known, or of more or less complex mixtures.

Accidental Poisoning.—The total deaths from accidental poisoning in England for the twenty-five years, 1848–1872, were 8,234, the distribution of sexes being—males, 4,792; females, 3,442. If calculated out in ratios of deaths from all causes, the proportions are—82 per million total deaths, males; 62 per million total deaths, females; or 19 per million of the living male population, and 13 of the living female population. The influence of age may be gathered from the following table, which gives the abstract numbers representing the relative probability of poisoning at the ages given of a million people in the period named:—

		Males.	Females.
Under 1 year,	.	141	113
" 5 years,	.	56	37
" 10 "	.	5	4
" 20 "	.	7	13
" 35 "	.	13	10
" 45 "	.	29	14
" 55 "	.	31	40
" 65 "	.	27	17
Above 45 "	.	22	27

Suicide by Poison.—During the nineteen years, 1853–1872, 5,566 females, and 15,340 males committed suicide. The different forms of death which these unfortunate persons chose may be tabulated thus:

MALES.

	Number.	Per Thousand.
Hanging,	6,821	444
Cutting, Stabbing,	8,189	208
Drowning,	2,094	186
Otherwise,	1,199	78
Poison,	1,110	72
Gunshot,	987	62

FEMALES.

Hanging,	1,665	299
Drowning,	1,618	290
Poison,	900	162
Cutting,	890	160
Otherwise,	488	87
Gunshot,	12	2

Methods of suicide adopted by 1,000 males and females in Great Britain per 1,000 of each sex, 1871-80 :—

	Males.	Females.
Hanging, Strangulation,	399.8	268.1
Cut, Stab, or other Wound,	212.0	147.9
Drowning,	165.5	333.8
Poison,	78.9	172.2
Gunshot,	67.8	2.3
Lying on Rail, or Jumping from the Train,	28.6	7.6
Jumping from Height	20.5	35.9
Otherwise,	31.9	82.7

Hanging, then, appears to be the most favoured mode of death, but with regard to other violent causes of decease, the different habits of life and formation of the two sexes cause a considerable difference. A woman is not accustomed to firearms, and has seldom access to them ; she is also averse to cutting instruments ; hence "*cutting and stabbing*," occupying the second place in order of frequency among the male suicides, diminishes to the fourth place among the female, while the item "*gunshot wounds and wounds by firearms generally*," although occupying the place of least frequency in both sexes, yet accounts for more than sixty per thousand of the males, and only two per thousand of the females. Death by poison is third in the list of female suicides, and fourth among males ; this, again, is evidently due to the mental peculiarities of the two sexes, and in part also, perhaps, to the superior facilities of the male in the possession of destructive weapons. However this may be, it is evident from the statistics quoted that, among English people, a suicidal woman is twice as likely to take poison as a

suicidal man. Whether this ratio would hold good if the statistics were drawn entirely from the educated ranks of society is perhaps doubtful. Very similar results are brought out by Fircks in his Prussian statistics.*

TABLE IV.—SHOWING THE PREDILECTION OF 1000 PRUSSIAN SUICIDES FOR VARIOUS FORMS OF VIOLENT DEATHS FOR THE SEVEN YEARS 1869-1875.

	Males.	Females.
Hanging,	647·19	441·95
Drowning,	137·89	406·06
Poison,	18·31	65·45
Cut-throat,	30·52	31·76
Firearms,	129·77	5·82
Suicide by placing themselves on the Railway, . . .	14·46	13·59
Fall from a Height,	6·34	13·81
Opening of the Veins,	5·16	5·09
Breathing Poisonous Gases,	1·42	8·73
Stabbing,	3·76	3·88
Strangling,	2·79	2·18
Cutting the Abdomen,	·59	·72
Other ways, and unclassed	1·80	·96

Poison in the Prussian statistics occupies the third place, as in England; but the effect of a military education, and the constant handling of firearms, causes the deaths of suicidal males by gun or pistol shot, instead of occupying, as in England, the *last* place in order of frequency, actually to stand third in the list, and to account for nearly 130 per thousand of the total violent deaths.

CRIMINAL POISONING.

Some useful statistics of criminal poisoning have been given by Tardieu† for the 21 years, 1851-1871, which may be summarised as follows:

* *Rückblick auf die Bewegung der Bevölkerung im Preussischen Staate während des Zeitraumes vom Jahre 1816, bis zum Jahre 1844, in Nro. 48 der Preussischen Statistik, herausgegeben vom Königl. statistischen Bureau in Berlin, 1879, 4, S. 123.*

† “*Étude Médico-Légale sur l’Empoisonnement.*” Paris, 1875.

Total Accusations of Poisoning in the 21 years, 798

RESULTS OF THE POISONING :—

Death,	280	872
Illness,	346	
Negative,	246	

ACCUSED :—

Men,	904	708
Women,	899	

NATURE OF POISON EMPLOYED :—

Arsenic	287
Phosphorus,	267
Copper { Sulphate,	120
Acetate (Verdigris),	89
Sulphuric Acid,	86
Acids { Hydrochloric Acid,	8
Nitric Acid,	8
Cantharides,	80
Nux Vomica,	5
Strychnine,	7
Opium,	6
Opiates { Laudanum,	8
Sedative Water,	1
Salts of Mercury,	8
Sulphate of Iron,	6
Preparations of Antimony,	5
Ammonia,	4
Cyanides { Prussic Acid,	2
Cyanide of Potash,	2
Hellebore,	8
Datura Stramonium,	8
Powdered Glass,	8
Digitalin,	2
Potash,	2
Sulphate of Zinc,	2
Eau de Javelle (a solution of Hypochlorite of Potash,	1
Tincture of Iodine,	1
Croton Oil,	1
Nicotine,	1
Belladonna,	1
“ Baume Fiovarenti,”	1
Euphorbia,	1
Acetate of Lead,	1
Carbonic Acid Gas,	1
Laburnum Seeds,	1
Colchicum,	1
Mushrooms,	1
Sulphuric Ether,	1
Total,	867

It hence may be concluded, according to these statistics of criminal poisoning, that of 1000 attempts in France, either to injure or destroy human life by poison, the following is the most probable selective order:—

Arsenic,	331
Phosphorus,	301
Preparations of Copper,	183
The Mineral Acids,	54
Cantharides,	35
Strychnine,	14
Opiates	12
Mercurial preparations,	9
Antimonial preparations,	6
Cyanides (that is, Prussic Acid and Potassic Cyanide),	5
Preparations of Iron,	5

This list accounts for 995 poisonings, and the remaining 45 will be distributed among the less-used drugs and chemicals.

IV.—THE CONNECTION BETWEEN TOXIC ACTION AND CHEMICAL COMPOSITION.

The therapeutic or poisonous action of a newly discovered compound can only be found in testing it with life. This “*life-test*” is also from time to time necessary to identify certain substances, the chemical reactions of which are inferior to, or more obscure than, their physiological effects. No great generalisation has yet been propounded by which, from the chemical composition of a given substance, we can predicate its physiological action; but work has been done in this direction which gives reason to expect that it will ultimately be accomplished. Drs. Crum Brown and Fraser* have suggested that there is some relation between toxicity and the saturated or non-saturated condition of the molecule. For example, kakodylic acid† is inert and tetramethyl stibonium has no emetic properties; these are all saturated compounds; but, on the other hand, there are several exceptions; such, *e.g.*, as alcohol, oxalic acid, and corrosive sublimate. The experiment of introducing

* “On the Connection between Chemical Constitution and Physiological Action, with special reference to the physiological action of the Ammonium Bases, derived from Strychnine, Brucine, Thebaine, Codeine, Morphine, and Nicotine.” By A. Crum Brown, M.D., D.Sc., F.R.S.E., and T. B. Fraser, M.D., F.R.S.E. *Journ. Anat. and Phys.*, vol. ii., p. 224.

† Bunsen: *Annalen der Chimie u. Pharm.* xlvi. 10.

methyl into strychnine led to some interesting results. (See article "Strychnine.")

M. Ch. Michet* has investigated the comparative toxicity of the metals by experiments on fish, using species of *serranus*, *crenolabrus*, and *julis*. The chloride of the metal was dissolved in water and diluted until just that strength was attained in which the fish would live 48 hours; this, when expressed in grammes per litre, he called "the limit of toxicity."

The following is the main result of the inquiry, by which it will be seen that there was found no relation between "the limit of toxicity," and the atomic weight.

TABLE V.—EXPERIMENTS ON FISH.

No. of Experiments.	Metal.	Limit of Toxicity.
20.	Mercury	.00029
7.	Copper	.0033
20.	Zinc	.0084
10.	Iron	.014
7.	Cadmium	.017
6.	Ammonium	.064
7.	Potassium	.10
10.	Nickel	.126
9.	Cobalt	.126
11.	Lithium	.8
20.	Manganese	.30
6.	Barium	.78
4.	Magnesium	1.5
20.	Strontium	2.2
5.	Calcium	2.4
6.	Sodium	24.17

V.—LIFE-TESTS; OR, THE IDENTIFICATION OF POISON BY EXPERIMENTS ON ANIMALS.

A philosophical investigation of poisons demands a complete methodical examination into their action on every life form, from the lowest to the highest. Our knowledge is more definite with regard to the action of poisons on man, dogs, cats, rabbits, and frogs than on any other species. It may be convenient here to make a few general remarks as to the action of poisons on infusoria, the cephalopoda, and insects.

*"De la Toxicité comparée des différents Métaux." Note de M. Ch. Michet. Compt. Rend., t. xciii., 1881, p. 649.

Infusoria.—The infusoria are extremely sensitive to the poisonous alkaloids and other chemical agents. Such tiny lives are, for the most part, ever at hand; the nearest pool of stagnant water will furnish them in abundance, or they may be produced at home by steeping bread or meal for a few days in spring or river water kept at a temperature of from 15° to 18° . Strong doses of the alkaloids cause a contraction of the cell contents, and somewhat rapid disintegration of the whole body; moderate doses at first quicken the movements, then the body gets perceptibly larger, and finally, as in the first case, there is integration of the animal substance.

Rossbach* gives the following intimations of the proportion of the toxic principle necessary to cause death:—Strychnine 1 part dissolved in 1500 of water; veratrine 1 in 8000; quinine 1 in 5000; atropine 1 in 1000; the mineral acids 1 in 400-600; salts 1 in 200-300.

The extraordinary sensitiveness of the infusoria, and the small amount of material used in such experiments, would be practically useful if there were any decided difference in the symptoms produced by different poisons. But no one could be at all certain of even the class to which the poison belongs were he to watch, without a previous knowledge of what had been added to the water, the motions of poisoned infusoria. Hence the fact is more curious than useful.

Cephalopoda.—The action of a few poisons on the cephalopoda has been investigated by M. E. Yung.† Curara placed on the skin had no effect, but on the branchiae led to general paralysis. If given in even fifteen times a greater dose than necessary to kill a rabbit, it was not always fatal. Strychnine, dissolved in sea-water, in the proportion of 1 to 30,000, causes most marked symptoms. The first sign is relaxation of the chromataphore muscle and the closing of the chromataphores; the animal pales, the respiratory movements become more powerful, and at the end of a notable augmentation in their number, they fall rapidly from the normal number of 25 to 5 a minute. Then tetanus commences after a time, varying with the dose of the poison; the arm stiffens and extends in fan-like form, the entire body is convulsed, the respiration is in jerks, the animal empties his pouch, and at the end of a few minutes is dead, in a state of great muscular rigidity. If at this moment it is opened, the venous heart is found still beating. Nicotine and other poisons were experimented with, and the cephalopoda were found to be generally sensitive to the active alkaloids, and to exhibit more or less marked symptoms.

Insects.—I devoted considerable time, in the autumn of 1882, to observations on the effect of certain alkaloids on the common blow-fly,

* N. J. Rossbach, *Pharm. Zeitschr. für Russland*, xix, 628.

† *Compt. Rend.*, t. xci., p. 306.

thinking it possible that the insect would exhibit a sufficient series of symptoms of physiological phenomena to enable it to be used by the toxicologist as a living re-agent. If so, the cheapness and ubiquity of the tiny life during a considerable portion of the year would recommend it for the purpose. The results, on the whole, came up to my expectations, and, provided two blow-flies are caught and placed beneath glass shades—the one poisoned, the other not—it is surprising what a variety of symptoms can, with a little practice, be distinguished. Nevertheless, the absence of pupils, and the want of respiratory and cardiac movements, are, in an experimental point of view, defects for which no amount or variety of merely muscular symptoms can compensate.

From the nature of the case we can only distinguish in the poisoned fly dulness or vivacity of movement, loss of power in walking on smooth surfaces, irritation of the integument, disorderly movements of the limbs, protrusion of the fleshy proboscis, and paralysis, whether of legs or wings. My experiments were chiefly made by smearing the extracts or neutral solutions of poisons on the head of the fly. In this way some of it is invariably taken into the system, partly by direct absorption, and partly by the insect's efforts to free itself from the foreign substance, in which it uses its legs and proboscis. For the symptoms witnessed after the application of saponine, digitalin, and aconitine, the reader is referred to the articles on those substances.

In poisoning by sausages, bad meat, aconitine, curarine, and in obscure cases generally, in the present state of science, experiments on living animals are absolutely necessary. In this, and in this way only, in very many instances, can the expert prove the presence of zymotic, or show the absence of chemical poison.

Methods.—The simplest method of experiment on animals is one of high antiquity: some domestic animal, such as a dog or cat, is induced to eat part of the "substance suspect" by mixing it with his food. If the animal eat and live, the substance is innocent; if he eat and die, there is something wrong. By modern and more scientific methods, solutions of poisons are injected directly into the circulation or beneath the skin, the latter method being nearly always the more convenient. A small glass syringe, provided with a hollow needle, is charged, and the operator injects under the skin a known quantity of the solution, and watches the effects. An experimenting in this way on small animals such as mice, the needle, however fine, is, considering the size of the animal, really of the proportional dimensions of a spear to man, and effects are produced by the wound itself. Hence, it is more prudent in this instance to take two mice and inject under the skin of the one the liquid, the properties of which are sought, and under the skin of the other an equal bulk of pure water. Both mice having then been wounded in a similar place and man-

ner, but with syringes differently charged, are strictly comparable, and the error of confusing the mere effects of the operation with that of a poison is not likely to happen. The best seat for subcutaneous injection is the skin at the back of the neck, which in all animals is there a little loose. The situation is the more convenient, since cats and dogs taken up by firmly grasping this loose skin are unable to turn and bite. The operation itself presents no difficulty. If material suffice, it may be desirable to make several experiments on different classes of animals, and when this is the case, the cat, the rabbit, and the frog are, all things considered, the best subjects for selection.

In making experiments on animals, the amount or dose of the poison used, the time of its administration, and the time of occurrence of any symptoms should be accurately noted. The disturbances or deviations from the normal state, known as symptoms, may be conveniently divided into groups :—1. Symptoms referable to the respiratory system. 2. Disorder of the circulation : condition of the heart and arteries. 3. Nervous system : dilation or contraction of the pupils, paralysis, or convulsions, &c. 4. Effects on the muscular system. 5. Temperature. 6. Disorders of the digestive tract : vomiting, diarrhoea.

Respiration.—The number of respirations per minute is for the most part readily obtained by simple observation of the walls of the chest or of the nostrils of most animals. To observe the respiration of the frog, it is placed on its back, then the skin below the epi-sternal cartilage is seen to rise and fall at intervals, in health, of from one to two seconds.

There are instruments by which the movements of the chest can be recorded upon a revolving cylinder, and in investigating new poisons, such methods are preferable and far more accurate than any other. The respiration of poisoned animals may be slow, quick, shallow, gasping, intermittent, or spasmodic.

It is most important to note whether the respiration and the heart's action are both extinguished simultaneously, or nearly so, or whether the heart goes on beating after the respiration has ceased ; and, further, whether (as in many cases) life can be maintained by artificial respiration.

If artificial respiration is only required for a limited time, it is easily effected by introducing into the trachea of the animal a tracheal canula, attached to which should be the india-rubber tube connected with the common blower and expanding regulator found in almost all laboratories, and used for the purposes of the gas blow-pipe : if artificial respiration, however, is required for any length of time, then an automatic apparatus is in every respect more convenient. One of the best self-acting mechanisms is formed by a Sprengel's blow-pipe and an electrical apparatus for permitting the air to go in regular waves. A long tube (see fig.

1) having a side branch, F, is attached, on the one hand, to the water supply, and, on the other, is inserted by means of caoutchouc cork into a bottle, B, containing some water, the tube, A, dipping beneath the surface of the water. The cork is doubly perforated, and in the second

perforation there is a tube, X, bent at right angles to deliver the air. A current of water passing down A, sucks air in by F; the air is compressed in the bottle, and escapes by the right-angled tube, X, in a continuous stream; by suitable regulations of the taps, and especially of the clip, C, the same quantity of water is allowed to escape as that which enters the bottle, and thus a constant level is maintained. The current of air is broken in the following way (see fig. 2). F is a flat india-rubber bag, which is connected to the right-angled tube, X, of fig. 1 by a flexible tube b'; on b' is a weight closing it, but lifted off each time the current passes through an electro-magnet, falling when the current is broken; the interruption of the current is effected by a mercurial breaker, consisting of a U tube, c, containing mercury in the bend and resting on the bag, being in a vertical position beneath the arch of a little wooden bridge. The bridge supports two wires, d, d, insulated from one another; each wire is received into a limb of the U tube, and in this way, if the bag expands, the mercury touches the wires, and instantly the magnet lifts off the weight, and the air streams into the animal's lungs; the caoutchouc bag collapsing, the contact of wire and mercury is broken, and the weight falls, which, occluding the tube, permits distension of the bag to again occur. When properly adjusted, the machine requires very little attention.

2. *Circulation.*—Poisons often cause changes in the calibre of the smaller arteries, and such changes may be seen by examining the suitably prepared omentum of the living guinea-pig, or in the retinal vessels of man or of the larger animals. A still more convenient source of information is the web of the frog's foot, although this is suitable for viewing capillary vessels rather than small arteries. The heart itself is, however, the most important organ to which the toxicologist directs his attention,



Fig. 1.

more especially as a large class of poisons (of which digitalin is the type) appear to act primarily on the heart, and are hence called "heart poisons." The mere movements of the heart, the number and regularity or irregularity of its pulsations, as well as its force, can be with considerable ease ascertained by inspection and palpation in most animals; but in order to obtain precise information as to whether a given extract or poison acts specifically on the heart, it is necessary to expose the organ in such a manner that the details of its action can be observed by the aid of

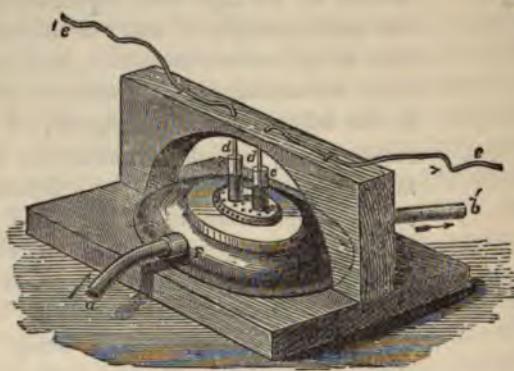


Fig. 2.

appliances, such as levers, kymographs, &c. For observations on the heart, that of the frog is most suitable, for it may be even removed from the body and solutions applied to its substance.

In removing the heart of a frog, the animal is first pithed to destroy all sensibility; the heart is then excised and placed in a watch-glass containing either serum or a solution of common salt, strength .75 per cent. Under these conditions the heart will go on beating for many hours, and if extracts or solutions containing poisonous matters be applied to its substance, changes will occur in the strength, number, or regularity of the pulsations. Thus, digitalin and the digitalin class may be studied and detected, and the antagonism of certain poisons may be demonstrated—*e.g.*, a drop of a solution of muscarine placed on the excised heart of the frog causes the pulsations to stop suddenly; but if to the heart thus stilled a drop of atropine is added, the beats recommence. Dr. Brunton observed this phenomenon after a frog's heart had ceased to beat for four hours. The unassisted eye will miss many of the peculiarities of the beats of the excised heart, and it is usual to make the contractions more evident by mechanical appliances.

A very simple form of lever, which can be made by any one, has been suggested by Dr. Brunton.* On a plate of glass, 3-4 inches long and 2 wide, is cemented a square piece of cork, the cork projecting half-an-inch beyond the plate. A little piece of light wood, 3 inches long, a quarter of an inch broad, and one-eighth of an inch thick, forms a lever, and works on a pin thrust through the lever into the cork. The lever is prolonged by a fine bonnet-straw, and carries a brush dipped in ink or other marking pencil; it can be fixed on to the lever by sealing-wax. By suitably weighting the lever, it can be made to move by the slightest impulse. The thick end of the lever is placed on the isolated heart, and if the pencil impinges upon a revolving cylinder, a graphic representation of the heart's action is obtained.

Arterial Pressure.—No scientific investigation of the action of poisons is complete without determinations of the arterial pressure. The simplest method of doing this is to connect an artery with a mercurial manometer, which in its most primitive form, consists of a U tube containing mercury. The pressure causes the fluid metal to be depressed in one limb, and to be elevated in the other; and if, on the surface of

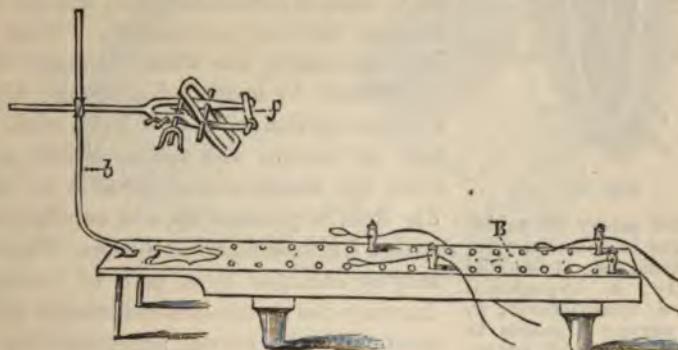


Fig. 3.

the metal in the latter limb, a float, with a long stem carrying a pencil, is placed on a short limb at right angles, the movements of the variations of pressure admit of graphic representation on a cylinder moved by clock-work.

The arteries selected for the determination of pressure are nearly always the carotid or the crural. The steps to expose these arteries, in operating with a rabbit, may be briefly detailed. The animal is most conveniently secured on an ingenious support known as Czermac's Rabbit-

* "A Simple Method of Demonstrating the Effect of Heat and Poisons upon the Heart of a Frog." By T. L. Brunton, M.D., F.R.S.—*Journ. Anatom. and Physiol.*, vol. x., p. 603.

Holder, (see fig. 3.) ; this consists of a stout board, B, 8 inches wide by 30 inches long. At one end there is an upright, *b*, on which a horizontal rod, carrying a peculiar sort of forceps, *f*, slides up and down, and between the blades of this apparatus the head of a rabbit, or other animal similar in size, can be held without injuring it. Along the edges of the board are convenient attachments for the extremities. In the absence of Czermac's apparatus, a deal board, into which brass-headed nails can be driven, will answer the purpose. The four legs, the body, and the head can be thus secured by means of tapes, the latter being attached to the

nails. To expose the carotid it is essential that the head should be well bent back, so as to fully bare the throat, and it will be found convenient for this purpose to utilise the rodent teeth of the upper jaw by attaching a ligature to the upper jaw, using the teeth as a point of attachment. The fur on the neck having now been cut very short, the skin just over the edge of the trachea is raised so as to make a horizontal fold, and an incision is made, vertical in direction. When bleeding has ceased, the wound through the skin is cleansed by means of a sponge dipped in a little solution of salt. Next, with a blunt pair of forceps, the fascia, which stretches from the sterno-mastoid muscle to the middle line, is pinched up, and carefully divided with a knife or a pair of scissors. The opening may be enlarged by a pair of forceps. On drawing the sterno-mastoid muscle aside, the artery and the nerves accompanying it will come into view (see fig. 4). The sheath of the artery is opened carefully, the artery caught up on a blunt hook, and the tube cleared for three-quarters of an inch in either direction. A ligature is now passed round the artery, and tied. On the heart side of this ligature, a slip of wood or cardboard is passed

Fig. 4.

Carotid artery of rabbit and parts in relation with it. *c*, carotid; *sh*, stylohyoid muscle; *h*, hypoglossal nerve; *s*, sympathetic; *v*, vagus nerve; *i*, points to superior laryngeal nerve, where it passes behind the carotid, close to its origin from the vagus; *p*, pharyngeal artery; *sm*, edge of sterno-mastoid muscle; *lh*, thyroid artery; *sth*, sterno-hyoid muscle; *l*, laryngeal artery—the nerve which crosses it is the descendens noni.

underneath the artery, and another ligature applied but quite loosely. A little clip is now made to occlude the artery on the cardiac side of the piece of wood, and with a pair of scissors a V-shaped cut is made ; into this cut a glass arterial canula* is inserted, and the

* The arterial canula is a T-shaped tube of glass, one arm of which, that, namely, to be inserted into the artery, is drawn out and bevelled. A second arm is connected with the manometer ; the third is furnished with a little caoutchouc tube and closed by a clip.

loose ligature slipped over it and tied securely. The preparation of the crural artery is as follows: a fold of skin in the inner surface of the thigh, almost exactly in the centre of Poupart's ligament, is pinched up and divided; the pulsation of the artery is readily felt by applying the finger in the hollow between the adductor muscles and those which cover the femur. The sheath of the vessels having been exposed, the crural nerve, the crural vein, and the artery will be seen occupying the relative positions shown in the drawing (fig. 5.)

Whatever artery is opened, and connected with the canula, the next step is to connect it with the manometer. The arterial canula, as stated in the footnote, is a T-shaped glass tube. The bevelled end is tied in the artery; another limb is connected with a bottle containing a solu-

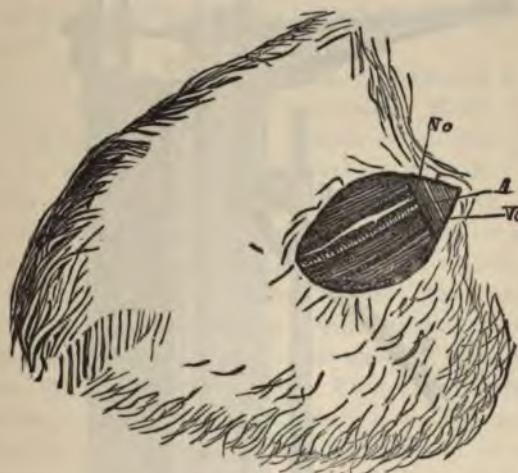


Fig. 5.

A, crural artery; *Vc*, crural vein, *Nc*, crural nerve.

tion of bicarbonate of soda by means of a long flexible tube guarded by a clip. The third leg or arm of the tube is to be connected with the manometer. The first step is to fill the tubes with bicarbonate of soda solution, and thus expel all air; this is effected by opening the clip communicating with the "pressure-bottle" of alkaline solution for a moment. When this has been done, and the tubes are filled with liquid, the free arm is connected with the manometer by means of a caoutchouc and a lead tube, the caoutchouc being used for connections only, because its elasticity interferes a little with the experiment. All is now ready, and the clip which has compressed the artery may be removed; the mercurial

column at once begins to oscillate, but no record should be taken for the first few seconds. After one or two minutes, a poison may be introduced by subcutaneous injection, and the effect watched.

Much may be learnt by the aid of the simple recording cylinder, or even by a graduated manometer, and the reading of the number of millimetres through which the mercury rises and falls. It is, however, far

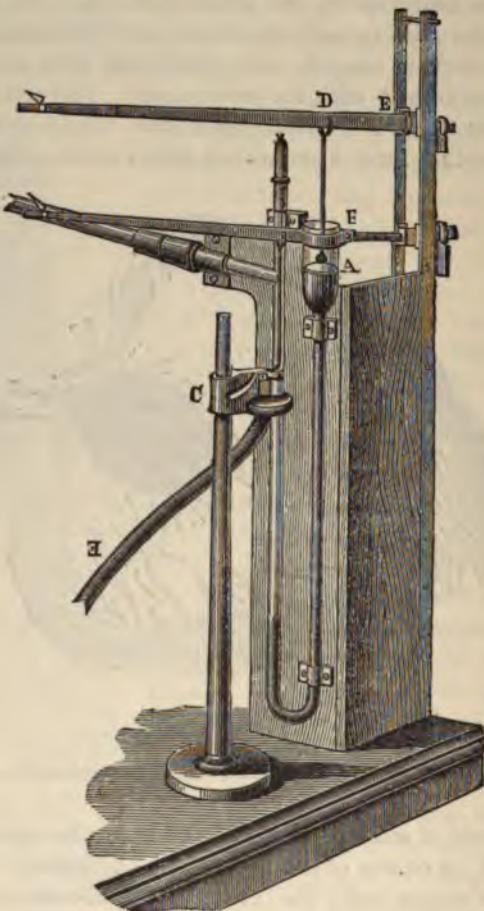


Fig. 6.

preferable in experiments of this kind to obtain a graphic representation both of the respiration and pressure simultaneously. A very good form of instrument by which this may be effected is described by Dr. Burdon Sanderson* (see fig. 6). The mercurial manometer consists of two limbs

* "Handbook of the Physiological Laboratory," p. 315. London, 1873. The illustration has been taken from the same work.

of equal length, one of which, the distal end, A, is near the top much wider than the other, the relation between the lumen of the one and that of the other being as 1 : 10. The float which rests on the distal column is of box-wood ; its under surface is concave, so as to fit the convex surface of the mercury ; by the vertical rod it is connected with the light lever D, about two feet in length, which is counterpoised by a weight suspended to it on the other side of the brass bearing, E. At this thin end, the lever carries a pin, the distance of which is such that, for every inch of variation of difference between the two columns of the manometer, it rises or falls three-tenths of an inch. It will be readily understood that the movement of the pin, instead of being rectilinear, is circular ; consequently, it is vertical only when the lever is horizontal ; for which reason the fulcrum, E, which is so constructed as to slide up and down on the brass uprights, must always be placed in such a position that the lever is horizontal.

The height of the mercurial column corresponds to the average arterial pressure. That part of the instrument which is intended for recording the respiratory movements consists of a Marey's tympanum, C, and a lever, F, similar to D and of the same length, with which it is connected. The tube, H, of the tympanum must be either brought into communication with one arm of a glass, T, tube, the stem of which is inserted into the trachea, or with a stethometer applied to the chest. The lever of the tympanum is connected with the recording lever as shown in the figure. In this way two tracings, the one of the respiration, the other of the arterial pressure, are obtained simultaneously.

3. *Nervous System.*—Contraction or dilatation of the pupils, disordered movements, convulsions, paralysis, tetanic spasms, and similar symptoms referable to the nervous system, are evident enough, and seen without mechanical aids ; but there are questions to be solved that entail delicate manipulation and require the assistance of instruments of precision ;—e.g., in poisons like urari, which paralyse the muscular system, the question to be solved is whether the muscular irritability is destroyed or the function of the nerves suspended. To ascertain this, a frog under the full influence of urari (that is, with all the voluntary muscles paralysed, but with the heart still beating), should be taken, and the sciatic nerve exposed in the thigh ; a pair of electrodes, resting on a thin sheet of india-rubber, in order to prevent the current passing into the neighbouring muscles, is slipped under the nerve. On now sending an interrupted current through the nerve, no contraction of the muscles of the leg takes place. On the other hand, when the muscles themselves are stimulated they contract ; so it becomes evident that this particular poison suspends the function of the nerves, and does not destroy the muscular irritability. To find out whether a poison like

urari acts on the ends of the nerves, or on the trunk, the following experiment can be made. The gastrocnemius muscle of a frog is dissected out, and its blood-vessels ligatured; then the origin and insertion of the muscles are divided, and it is left attached to the body only by the nerve. On now poisoning with urari, it is found that a stimulus applied to the nerve causes contraction of the muscle, though all the other nerves of the body have lost their irritability. The presumption, then, is that urari acts only on the ends of the nerves.

Troubles of the sensorium, noises in the ears, flashes of light before the eyes, and disturbances of taste, are matters which can be only imperfectly investigated by experiments on the lower animals, and what we know of these symptoms is for the most part derived from observations on man; so, also, delicate variations in the sense of touch can only be properly ascertained by observations on man, but complete or partial loss of sensation can, of course, be readily determined by the application of stimuli to the extremities or skin of animals.



Fig. 7.

4. *Muscular System.*—The effect of poisons on muscle may often be conveniently studied by making what physiologists call a "nerve muscle preparation" (see fig. 7). This is done by carefully dissecting out the gastrocnemius of the frog with the sciatic nerves, S, dividing the latter close up to the spinal cord, and placing the muscle thus detached under a glass shade, or under any conditions by which it can be bathed in an atmosphere saturated with aqueous vapour. By attaching the end of the femur, F, to a fixed support, and the tendo-achilles, I, to a lever which may be weighted variously, and passing a current, both the force and duration of the muscular contraction may be ascertained and graphically recorded on a revolving cylinder. It is still more instructive to determine the tracing of the gastrocnemius of a living frog by first dividing the sciatic nerve, and then exposing the muscle, without severing its blood-supply from that of the rest of the body. Having obtained a normal tracing on the recording cylinder, the poison is injected underneath the skin on the frog's back, and it is noted whether the contractions are prolonged or shortened, weakened or strengthened.

The broad fact that a poison prolongs or retards, weakens or excites, muscular contraction can be ascertained by very simple means on the principles above detailed; but more elaborate researches (and especially those of a comparative nature) require apparatus of delicacy and costliness.

5. *Temperature.*—The temperature of mammals alone is of impor-

tance, as giving a clue to the action of a poison. The little clinical thermometers used by physicians answer every purpose. The temperature is best taken in the rectum, and that as frequently as possible. The results admit of graphical representation on the usual principles.

6. *Disorders of the Digestive Tract, &c.*—Affections of the digestive tract—e.g., loss of appetite, vomiting, and diarrhoea—will be noticed as common effects of all irritant poisons.

Cultivation of Bacilli, &c.—In cases in which there are reasonable grounds for supposing that a person is poisoned by a zymotic contagion, as, for example, in cases of illness after eating the meat of animals dying from anthrax or kindred maladies, it may be necessary to “cultivate” extracts of the meat eaten, or the blood of the person who has suffered, and make experiments on animals with the products of the cultivation. The apparatus for “cultivation” may be of a very simple character, the chief condition being some arrangement which will give a uniform temperature. A water-bath, formed by placing a large beaker in a small one, and filling each nearly full of water, makes a good incubator, and, if fitted with a Page’s gas-regulator, is capable of doing useful work. Page’s gas-regulator* is essentially a large thermometer, which may be so arranged that, when the temperature rises to a certain point, the mercury shuts off or diminishes the gas supply. I find that by its means a water-bath or incubator can be kept for weeks together without varying more than a degree. Cultivations may be carried on in test-tubes or little microscope cells. The best medium for the particular purpose in view is pure white of egg, though, in certain cases, it may be convenient to use milk, and in others blood.†

Single drops of the fluid to be cultivated are added to the nourishing fluid, and the temperature maintained at blood-heat (36.7°) for one, two or more days, the liquid from time to time being examined microscopically, and portions of it injected into small animals such as mice, and the effects noted.

* The apparatus may be obtained from Messrs. Cetti, Brook Street, Holborn, W. C.

† For *anthrax acillus*, and indeed for many others, Dr. Klein’s “gelatine pork,” made on Koch’s plan, is admirable. Very complete directions for making and sterilising the gelatine pork, etc., may be found in the Annual Report of the Local Government Board, Supplement, containing Report of the Medical Officer for 1881, p. 172.

VI.—GENERAL METHOD OF PROCEDURE IN SEARCHING FOR POISON.

Mineral substances or liquids containing only inorganic matters, can cause no possible difficulty to any one who is practised in analytical investigation ; but the substances which exercise the skill of the expert are organic fluids or solids.

The first thing to be done is to note accurately the manner in which the samples have been packed, whether the seals have been tampered with, whether the vessels or wrappers themselves are likely to have contaminated the articles sent ; and then to make a very careful observation of the appearance, smell, colour, and reaction of the matters, not forgetting to take the weight, if solid—the volume, if liquid. All these are obvious precautions, requiring no particular directions.

If the object of research is the stomach and its contents, the contents should be carefully transferred to a tall, conical glass ; the organ cut open, spread out on a sheet of glass, and examined minutely by a lens, picking out any suspicious-looking substance for closer observation. The mucous membrane should now be well cleansed by the aid of a wash-bottle, and if there is any necessity for destroying the stomach, it may be essential in important cases to have it photographed. The washings having been added to the contents of the stomach, the sediment is separated and submitted to inspection, for it must be remembered that, irrespective of the discovery of poison, a knowledge of the nature of the food last eaten by the deceased may be of extreme value.

If the death has really taken place from disease, and not from poison, or if it has been caused by poison, and yet no definite hint of the particular poison can be obtained either by the symptoms or by the attendant circumstances, the analyst has the difficult task of endeavouring to initiate a process of analysis which will be likely to discover any poison in the animal, vegetable, or mineral kingdom. For this purpose I have devised the following process, which differs from those that have hitherto been published mainly in the prominence given to operations in a high vacuum, and the utilisation of biological experiment as a matter of routine. Taking one of the most difficult cases that can occur—viz., one in which a small quantity only of an organic solid or fluid is available—the best method of procedure is the following :—

A small portion is reserved and examined microscopically, and, if thought desirable, submitted to various “cultivation” experiments in the manner described (p. 49). The greater portion is at once examined for volatile matters, and having been placed in a strong flask, and, if neutral or alkaline, feebly acidulated with tartaric acid, connected with

a second or receiving-flask by glass tubing and caoutchouc corks. The caoutchouc cork of the receiving-flask has a double perforation, so as to be able, by a second bit of angle tubing, to be connected with the mercury pump described in vol. i., "Foods," p. 70, the figure of which is here repeated (see fig. 8). A vacuum having been obtained, and the receiving-flask surrounded with ice, a distillate for preliminary testing may be generally got without the action of any external heat; but if this is too slow, the flask containing the substances or liquid under examination may be gently heated by a water-bath—water, volatile oils, a variety of volatile substances, such as prussic acid, hydrochloric acid, phosphorus, &c., if present, will distil over. It will be well to free in this way the substance, as much as possible, from volatile matters and water. When no more will come over, the distillate may be carefully examined by redistillation and the various appropriate tests.

The next step is to dry the sample thoroughly. This is best effected also in a vacuum by the use of the same apparatus, only this time the receiving-flask is to be half filled with strong sulphuric acid. By now applying very gentle heat to the first flask, and cooling the sulphuric acid receiver, even such substances as the liver in twenty-four hours may be obtained dry enough to powder.

Having by these means obtained a nearly dry friable mass, it is reduced to a coarse powder, and extracted with petroleum ether; the extraction may be effected either in a special apparatus (as, for example, in a large "Soxhlet"), or in a beaker placed in my "Ether recovery apparatus" (see fig. 9), which is adapted to an upright condenser. The petroleum extract is evaporated and leaves the fatty matter, possibly contaminated by traces of any alkaloid which the substance may have contained; for although most alkaloids are insoluble in petroleum ether, yet they are taken up in small quantities by oils and fats, and are extracted with the fat by petroleum ether. It is hence necessary always to examine the petroleum extract by shaking it up with water, slightly acidulated with sulphuric acid, which will extract from the fat any trace

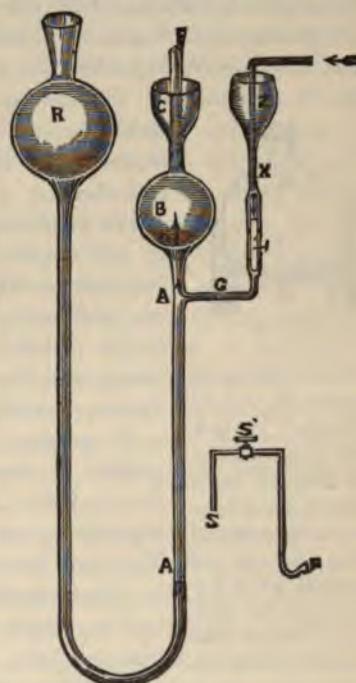


Fig. 8.

of alkaloid, and will permit the discovery of such alkaloids by the ordinary "group re-agents."

The substance now being freed for the most part from water and from fat is digested in the cold with absolute alcohol for some hours; the alcohol is filtered off, and allowed to evaporate spontaneously, or, if speed is an object, it may be distilled *in vacuo*. The treatment is next with hot alcohol of 90 per cent., and, after filtering, the dry residue is exhausted with ether. The ether and alcohol, having been driven off, leave extracts which may be dissolved in water and tested both chemically and biologically, for alkaloids, glucosides, and organic acids. It must also be remembered that there are a few metallic compounds (as for example, corrosive sublimate) which are soluble in alcohol and ethereal solvents, and must not be overlooked.

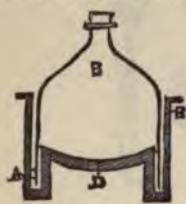


Fig. 9.

This figure is from p. 70, vol. i., "Foods." B is a bell-jar, which can be adapted by a cork to a condenser; R is made of iron; the rim of the bell-jar is immersed in mercury, which the deep groove receives.

If arsenic, in the form of arsenious acid, were present, it would distil over as a trichloride, and be detected in the distillate; by raising the heat, the organic matter is carbonised, and most of it destroyed. The distillate is saturated with hydric sulphide, and any precipitate separated and examined. The residue in the retort will contain the fixed metals, such as zinc, copper, lead, &c. It is treated with dilute hydrochloric acid, filtered, the filtrate saturated with SH_2 , and any precipitate collected. The filtrate is now treated with sufficient sodic acetate to replace the hydric chloride, again saturated with SH_2 , and any precipitate collected and tested for zinc, nickel, and cobalt. By this treatment, viz:—

1. Distillation in a vacuum at a low temperature,
2. Collecting the volatile products,
3. Dehydrating the organic substances,
4. Dissolving out from the dry mass fatty matters and alkaloids, glucosides, &c., by ethereal and alcoholic solvents,
5. Destroying organic matter and searching for metals,

—a very fair and complete analysis made be made from a small amount

of material. The process is, however, somewhat faulty in reference to phosphorus, and also to oxalic acid and the oxalates ; these poisons, if suspected, should be specially searched for in the manner to be more particularly described in the sections treating of them. In most cases, there is sufficient material to allow of division into three parts—one for organic poisons generally, one for inorganic, and a third for reserve in case of accident. When such is the case, although, for organic principles, the process of vacuum distillation just described still holds good, it will be very much the most convenient way not to use that portion for metals, but to operate on the portion reserved for the inorganic poisons as follows by destruction of the organic matter.

The destruction of organic matter through simple distillation by means of pure hydrochloric acid, is at least equal to that by sulphuric acid, chlorate of potash, and the carbonisation methods. The object of the chemist not being to dissolve every fragment of cellular tissue, muscle, and tendon, but simply all mineral ingredients, the less organic matter which goes into solution the better. That hydrochloric acid would fail to dissolve sulphate of baryta and sulphate of lead, and that sulphide of arsenic is almost insoluble in the acid, is no objection to the process recommended, for it is always open to the analyst to treat the residue specially for these substances. The sulphides precipitated by hydric sulphide from an acid solution are—arsenic, antimony, tin, cadmium, lead, bismuth, mercury, copper, and silver. Those not precipitated are—iron, manganese, zinc, nickel, and cobalt.

As a rule, one poison alone is present ; so that if there should be a sulphide, it will belong only exceptionally to more than one metal.

The colour of the precipitate from hydric sulphide is either yellowish or black. The yellow and orange precipitates are sulphur, sulphides of arsenic, antimony, tin, and cadmium. In pure solutions they may be almost distinguished by their different hues, but in solutions contaminated by a little organic matter the colours may not be distinctive. The sulphide of arsenic is of a pale yellow colour ; and if the very improbable circumstance should happen that arsenic, antimony, and cadmium occur in the same solution, the sulphide of arsenic may be first separated by ammonia, and the sulphide of antimony by sulphide of sodium, leaving cadmic sulphide insoluble in both processes.

The black precipitates are—lead, bismuth, mercury, copper, and silver. The black sulphide is freed from arsenic, if present, by ammonia, and digested with dilute nitric acid, which will dissolve all the sulphides, save those of mercury, and tin, so that if a complete solution is obtained (sulphur flocks excepted), it is evident that both these substances are absent. The presence of copper is betrayed by the blue colour of the nitric acid solution, and through its special reactions ; lead, by

the deep yellow precipitate which falls by the addition of chromate of potash and acetate of soda to the solution ; bismuth, through a white precipitate on dilution with water. If the nitric acid leaves a black insoluble residue, this is probably sulphide of mercury, and should be treated with concentrated hydrochloric acid to separate flocks of sulphur evaporated to dryness, again dissolved, and tested for mercury by iodide of potash, copper, foil, &c., as described in the article on *Mercury*. Zinc, nickel, and cobalt are likewise tested for in the filtrate as described in the respective articles on these metals.

PART III.—ACIDS AND ALKALIES.

SULPHURIC ACID—HYDROCHLORIC ACID—NITRIC ACID—
AMMONIA—POTASH—SODA—NEUTRAL SODIUM, PO-
TASSIUM, AND AMMONIUM SALTS.

I.—SULPHURIC ACID.

Sulphuric acid (hydric sulphate, oil of vitriol, H_2SO_4) occurs in commerce in varying degrees of strength or dilution; the strong sulphuric acid of the manufacturer, containing 100 per cent. of real acid (H_2SO_4), has a specific gravity of 1.850. The ordinary brown acid of commerce, coloured by organic matter and holding in solution metallic impurities, chiefly lead and arsenic, has a specific gravity of about 1.750; contains 67.95 of anhydrous SO_3 —85.42 of hydric sulphate.

There are also weaker acids used in commerce, particularly in manufactories in which sulphuric acid is made, for special purposes without rectification. The British Pharmacopeia sulphuric acid is directed to be of 1.845 specific gravity, which correspond to 78.6 per cent. sulphuric anhydride, or 98.8 per cent. of hydric sulphate. The dilute sulphuric acid of the pharmacopeia should have a specific gravity of 1.094, and is usually said to correspond to 10.14 per cent. of anhydrous sulphuric acid; but, if Ure's Tables are correct, such equals 11.37 per cent.

The general characters of sulphuric acid are as follows:—When pure, it is a colourless, or, when impure, a dark brown to black, oily liquid, without odour at common temperatures, of an exceedingly acid taste, charring most organic tissues rapidly, and, if mixed with water, evolving much heat. If 4 parts of the strong acid are mixed with 1 part of water at 0°, the mixture rises to a heat of 100°; a still greater heat is evolved by mixing 75 parts of acid with 27 of water.

Sulphuric acid is powerfully hygroscopic—3 parts will, in an ordinary atmosphere, increase to nearly 4 in twenty-four hours; in common with all acids, it reddens litmus, yellows cochineal, and changes all vegetable colours. There is another form of sulphuric acid, extensively used in the arts, known under the name of "Nordhausen sulphuric acid," "fuming acid," formula $H_2S_2O_4$. This acid is produced by the distillation of dry ferrous sulphate, at a nearly white heat—either in

earthenware or in green glass retorts; the distillate is received in sulphuric acid. As thus manufactured, it is a dark fuming liquid of 1.9 specific gravity, and boiling at 53°. When artificially cooled down to 0°, the acid gradually deposits crystals, which consist of a definite compound of 2 atoms of anhydrous sulphuric acid and 1 atom of water. There is some doubt as to the molecular composition of Nordhausen acid; it is usually considered as hydric sulphate saturated with sulphur dioxide. This acid is manufactured chiefly in Bohemia, and is used, on a large scale, as a solvent for alizarine.

Sulphur Trioxide, or Sulphuric Anhydride (SO_3), itself may be met with in scientific laboratories, but is not in commerce. Sulphur trioxide forms thin needle-shaped crystals, arranged in feathery groups. Seen in mass, it is white, and has something the appearance of asbestos. It fuses to a liquid at about 18°, boils at 35°, but, after this operation has been performed, the substance assumes an allotropic condition, and then remains solid up to 100°; above 100° it melts, volatilises, and returns to its normal condition. Sulphuric anhydride hisses when it is thrown into water, chemical combination taking place and sulphuric acid being formed. Sulphur trioxide is excessively corrosive and poisonous.

Besides the above forms of acid, there is an officinal preparation called "Aromatic Sulphuric Acid," made by digesting sulphuric acid, rectified spirit, ginger, and cinnamon together. It contains 10.91 per cent. of SO_3 , alcohol, and principles extracted from cinnamon and ginger.

Sulphuric acid, in the free state, may not unfrequently be found in nature. I recently examined an effluent water from a Devonshire mine, which contained more than one grain of free sulphuric acid per gallon, and was accused, with justice, of destroying the fish in a river. It also exists in large quantities in volcanic springs. In a torrent flowing from the volcano of Parcé, in the Andes, Boussingault calculated that 15,000 tons of sulphuric acid and 11,000 tons of hydrochloric acid were yearly carried down. In the animal and vegetable kingdom, sulphuric acid exists, as a rule, in combination with bases, but there is an exception in the saliva of the *Dolium galea*, a Sicilian snail.

Statistics.—When something like 900,000 tons of sulphuric acid are produced annually in England alone, and when it is considered that sulphuric acid is used in the manufacture of most other acids, in the alkali trade, in the manufacture of indigo, in the soap trade, in the manufacture of artificial manure, and in a number of technical processes, there is no cause for surprise that it should be the annual cause of many deaths.

The number of deaths from sulphuric acid will vary, other things being equal, in each country, according to the manufactures in that

country employing sulphuric acid. In England, there are at least from thirty to forty poisonings yearly by sulphuric acid. Falck,* in comparing different countries, considers the past statistics to show that in France sulphuric acid has been the cause of 4·5 to 5·5 per cent. of the total deaths from poison, and in England 5·9 per cent. In England, France, and Denmark, taken together, 10·8, Prussia, 10·6; while in certain cities, as Berlin and Vienna, the percentages are much higher—Vienna showing 43·3 per cent., Berlin 90 per cent.

Accidental, Suicidal, and Criminal Poisoning.—Deaths from sulphuric acid are, for the most part, accidental, occasionally suicidal, and, still more rarely, criminal. In 53 out of 113 cases collected by Böhm, in which the cause of the poisoning could, with fair accuracy, be ascertained, 45·3 per cent. were due to accident, 30·2 were suicidal, and 54·5 per cent. were cases of criminal poisoning, the victims being children.

The cause of the comparatively rare use of sulphuric acid by the poisoner is obvious. First of all, the acid can never be mixed with food without entirely changing its aspect; next, it is only in cases of insensibility or paralysis that it could be administered to an adult, unless given by force, or under very exceptional circumstances; and lastly, the stains on the mouth and garments would at once betray, even to uneducated persons, the presence of something wrong. As an agent of murder, then, sulphuric acid is confined in its use to young children, more especially to the newly born.

There is a remarkable case related by Hagan,† in which an adult man, in full possession of his faculties, neither paralysed nor helpless, was murdered by sulphuric acid. The wife of a day labourer gave her husband drops of sulphuric acid on sugar, instead of his medicine, and finally finished the work by administering a spoonful of the acid. The spoon was carried well to the back of the throat, so that the man took the acid at a gulp. 11 grms. (171 grains) of sulphuric acid, partly in combination with soda and potash, were separated from his stomach.

Accidental poisoning is most common among children. The oily, syrupy-looking sulphuric acid, when pure, may be mistaken for glycerine or for syrup; and the dark commercial acid might, by a careless person, be confounded with porter or any dark-looking medicine.

Serious and fatal mistakes have not unfrequently arisen from the use of injections. Deutsch* relates how a midwife, in error, administered

* *Lehrbuch der Praktischen Toxicologie*, p. 54.

† Gross: *Die Strafrechtspflege in Deutschland*, 4, 1861. Heft. I. S. 181.

* *Preuss. Med. Vereins-Zeitung*, 1848, No. 13.

to mother and child a sulphuric acid clyster; but little of the fluid could in either case have actually reached the rectum, for the mother recovered in eight days, and in a little time the infant was also restored to health. Sulphuric acid has caused death by injections into the vagina. H. C. Lombard* observed a case of this kind, in which a woman, aged thirty, injected half a litre of sulphuric acid into the vagina, for the purpose of procuring abortion. The result was not immediately fatal, but the subsequent inflammation and its results so occluded the natural passage that the birth became impossible, and a Cæsarean section extracted a dead child, the mother also dying.

An army physician prescribed for a patient an emollient clyster. Since it was late at night, and the apothecary in bed, he prepared it himself; but not finding linseed oil, woke the apothecary, who took a bottle out of one of the recesses and placed it on the table. The bottle contained sulphuric acid; a soldier noticed a peculiar odour and effervescence when the syringe was charged, but this was unheeded by the doctor. The patient immediately after the operation suffered the most acute agony, and died the following day; before his death, the bed clothes were found corroded by the acid, and a portion of the bowel itself came away. †

Fatal Dose.—The amount necessary to kill an adult man is not strictly known; fatality so much depends on the concentration of the acid and the condition of the person, more especially whether the stomach is full or empty, that it will be impossible ever to arrive at an accurate estimate. Christison's case, in which 3·8 grms. (60 grains) of concentrated acid killed an adult, is the smallest lethal dose on record. Supposing that the man weighed 68½ kilo. (150 lbs.), this would be in the proportion of .05 grm. per kilo. There is also the case of a child of one year, recorded by Taylor, in which 20 drops caused death. If, however, it were asked in a court of law what dose of concentrated sulphuric acid would be dangerous, the proper answer would be: so small a quantity as from 2 to 3 drops of the strong undiluted acid might cause death, more especially if conveyed to the back of the throat; for if it is improbable that on such a supposition death would be sudden, yet there is a possibility of permanent injure to the gullet, with the result of subsequent contraction, and the usual long and painful malnutrition thereby induced. It may be laid down, therefore, that all quantities, even the smallest, of the *strong undiluted acid*, come under the head of hurtful, noxious, and injurious.

Local Action of Sulphuric Acid.—The action of the acid on living

* *Journ. de Chim. Méd.*, tom. vii. 1831.

† *Maschka's Handbuch*, p. 86. *Journal de Chimie Médicale*, t. i. No. 8, 405. 1835

animal tissues has been studied of late by C. Ph. Falck and L. Vietor.* Concentrated acid precipitates albumen, and then redissolves it ; fibrin swells and becomes gelatinous ; but if the acid is weak (e. g., 4 to 6 per cent.) it is scarcely changed. Muscular fibre is at first coloured amber-yellow, swells to a jelly, and then dissolves to a red-brown turbid fluid. When applied to the mucous membrane of the stomach, the mucous tissue and the muscular layer beneath are coloured white, swell, and become an oily mass.

When applied to the rabbit's ear,† the parenchyma becomes at first pale-grey and semi-transparent at the back of the ear ; opposite the drop of acid appear spots like grease or fat drops, which soon coalesce. The epidermis with the hair remains adherent ; the blood-vessels are narrowed in calibre, and the blood, first in the veins, and then in the arteries, is coloured green and then black and fully coagulates. If the drop, with horizontal holding of the ear is dried in, an inflammatory zone surrounds the burnt spot in which the blood circulates ; but there is complete stasis in the part to which the acid has been applied. If the point of the ear is dipped in the acid, the cauterised part rolls inwards ; after the lapse of eighteen hours the part is brown and parchment-like, with scattered points of coagulated blood ; then there is a slight swelling in the healthy tissues, and a small zone of redness ; within fourteen days a bladder-like, greenish-yellow scab is formed, the burnt part itself remaining dry. The vessels from the surrounding zone of redness gradually penetrate towards the cauterised spot, the fluid in the bleb becomes absorbed, and the destroyed tissues fall off in the form of a crust.

The changes that sulphuric acid cause in blood are as follows : the fibrin is at first coagulated and then dissolved, and the colouring matter becomes of a black colour. These changes do not require the strongest acid, being seen with an acid of 60 per cent.

The action of the acid on various non-living matters is as follows : poured on all vegetable earth, there is an effervescence, arising from decomposition of carbonates ; any grass or vegetation growing on the spot is blackened and dies ; an analysis of the layer of earth, on which the acid is poured, shows an excess of sulphates as compared with a similar layer adjacent ; the earth will only have an acid reaction, if there has been more than sufficient acid to neutralise all alkalies and alkaline earths.

Wood almost immediately blackens, and the spot remains moist.

Spots on paper become quickly dark, and sometimes exhibit a play

* *Deutsche Klinik*, 1863, Mo. 1-32, and Vietor's *Inaugur-Dissert.* Marburg, 1803.

† Samuel, *Entzündung u. Brand*, in *Virchow's Archiv f. Path. Anat.* Bd. 51. Hft. 1 u. 2, S. 41. 1870.

of colours, such as reddish-brown ; ultimately the spot becomes very black, and holes may be formed ; even when the acid is dilute, the course is very similar, for the acid dries in, until it reaches a sufficient degree of concentration to attack the tissue. I found small drops of sulphuric acid on a brussels carpet, which had a red pattern on a dark-green ground with light-green flowers, act as follows : the spots on the red at the end of a few hours were of a dark-maroon colour, the green was darkened, and the light-green, browned ; at the end of twenty-four hours but little change had taken place, nor could any one have guessed the cause of the spots without a close examination. Spots of the strong acid on thin cotton fabrics rapidly blackened, and actual holes were formed in the course of an hour ; the main difference to the naked eye, between the stains of the acid and those produced by a red-hot body, lay in the moistness of the spots. Indeed, the great distinction, without considering chemical evidence, between recent burns of clothing by sulphuric acid and by heat, is that in the one case—that of the acid—the hole or spot is very moist ; in the other, very dry. It is easy to imagine that this distinction may be of importance in a legal investigation.

Spots of acid on clothing fall too often under the observation of all those engaged in practical chemical work. However quickly a spot of acid is wiped off, unless it is immediately neutralised by ammonia, it ultimately makes a hole in the cloth ; the spot, as a rule, whatever the colour of the cloth, is of a blotting-paper red.

Sulphuric acid dropped on iron, attacks it, forming a sulphate, which may be dissolved out by water. If the iron is exposed to the weather, the rain may wash away all traces of the acid, save the corrosion ; but it would be under those circumstances impossible to say whether the corrosion was due to oxidation or a solvent.

To sum up, briefly: the characters of sulphuric acid spots on organic matters generally are black, brown, or red-coloured destructions of tissue, moisture, acid-reaction (often after years), and lastly, the chemical evidence of sulphuric acid or sulphates in excess.

Caution necessary in judging of spots, &c.—An important case, related by Maschka, shows the necessity of great caution in interpreting results, unless all the circumstances of a case be carefully collated. A live coal fell on the bed of a weakly infant, five months old. The child screamed, and woke the father, who was dozing by the fire ; the man, in terror, poured a large pot of water on the child and burning bed. The child died the following day.

A *post-mortem* examination showed a burn on the chest of the infant two inches in length. The tongue, pharynx, and gullet were all healthy ; in the stomach a patch of mucous membrane, about half an inch in extent, was found to be brownish, friable, and very thin. A chemical

examination showed that a portion of the bed adjacent to the burnt place contained free sulphuric acid. Here, then, was the following evidence: the sudden death of a helpless infant, a carbonised bed-cover, with free sulphuric acid, and, lastly, an appearance in the stomach which, it might be said, was not inconsistent with sulphuric acid poisoning. Yet a careful sifting of the facts convinced the judges that no crime had been committed, and that the child's death was due to disease. Afterwards, experiment showed that if a live coal fall on any tissue, and be drenched with water, free sulphuric acid is constantly found in the neighborhood of the burnt place.

Symptoms.—The symptoms may be classed in two divisions, viz.:—1. External effects of the acid. 2. Internal effects and symptoms arising from its interior administration.

1. *External Effects.*—Of late years several instances have occurred in which the acid has been used criminally to cause disfiguring burns of the face. The offence has in all these cases been committed by women, who, from motives of revengeful jealousy, have suddenly dashed a quantity of the acid into the face of the object of their resentment. In such cases, the phenomena observed are not widely different from those attending scalds or burns from hot neutral fluids. There is destruction of tissue, not necessarily deep, for the acid is almost immediately wiped off; but if any should reach the eye, inflammation, so acute as to lead to blindness, is the probable consequence. The skin is coloured at first white, at a later period brown, and part of it may be, as it were, dissolved. If the tract of skin touched by the acid is extensive, death may result. The inflammatory processes in the skin are similar to those noticed by Falck and Vietor in their experiments, already detailed (p. 59.)

2. *Internal Effects.*—When sulphuric acid is taken internally, the acute and immediate symptom is pain. This, however, is not constant, since, in a few recorded cases, no complaint of pain has been made; but these are quite exceptional, and, as a rule, there will be immediate and great suffering. The tongue swells, the throat is also swollen and inflamed, swallowing of saliva even may be impossible. If this acid has been in contact with the epiglottis and vocal apparatus, there may be spasmodic croup and even fatal spasm of the glottis.

The acid, in its passage down the gullet, attacks energetically the mucous membrane and also the lining of the stomach, but the action does not stop there, for Lesser found in 18 out of 26 cases (69 per cent.), that the corrosive action extended as far as the duodenum. There is excessive vomiting and retching; the matters vomited are acid, bloody, and slimy; great pieces of mucous membrane may be in this way expelled, and the whole of the lining membrane of the gullet may be

thrown up entire. The bowels are, as a rule, constipated, but exceptionally there has been diarrhoea; the urine is sometimes retained; it invariably contains an excess of sulphates and often albumen, with hyaline casts of the uriniferous tubes. The pulse is small and frequent, the breathing slow, the skin very cold and covered with sweat; the countenance expresses great anxiety, and the extremities may be affected with cramps or convulsions. Death may take place within from 24 to 36 hours, and be either preceded by dyspnoea or by convulsions; consciousness is, as a rule, maintained to the end.

There are also more rapid cases than the above; a large dose of sulphuric acid taken on an empty stomach may absolutely dissolve it, and pass into the peritoneum; in such a case there is really no difference in the symptoms between sudden perforation of the stomach from disease, a penetrating wound of the abdomen, and any other sudden fatal lesion of the organs in the abdominal cavity (for in all these instances the symptoms are those of pure collapse); the patient is ashen pale, with pulse quick and weak, the body bathed in cold sweat, and he rapidly dies, it may be without much complaint of local pain.

If the patient live longer than 24 hours, the symptoms are mainly those of inflammation of the whole mucous tract, from the mouth to the stomach; and from this inflammation the patient may die in a variable period, of from three to eleven days, after taking the poison. In one case the death occurred suddenly, without any immediately preceding symptoms rendering imminent death probable. If this second stage is passed, then the loss of substance in the gullet and in the stomach almost invariably causes impairment of function, leading to a slow and painful death. The common sequence is stricture of the gullet, combined with feeble digestion, and in a few instances stricture of the pylorus. A curious sequel has been recorded by Mannkopf, viz., obstinate intercostal neuralgia; it has been observed on the fourth, seventh, and twenty-second day.

Treatment of Acute Poisoning by the Mineral Acids.—The immediate indication is the dilution and neutralisation of the acid. For this purpose, finely divided chalk, magnesia, or sodic carbonate may be used, dissolved or suspended in much water. The use of the stomach-pump is inadvisable, for the mucous membrane of the gullet may be so corroded by the acid that the passage of the tube down will do injury; unless the neutralisation is *immediate*, but little good is effected; hence it will often occur that the bystanders, if at all conversant with the matter, will have to use the first thing which comes to hand, such as the plaster of a wall, &c.; and lastly, if even these rough antidotes are not to be had, the best treatment is enormous doses of water, which will dilute the acid and promote vomiting. The treatment of the after-

ffects belongs to the province of ordinary medicine, and is based upon general principles.

Post-mortem Appearances.—The general pathological appearances to be found in the stomach and internal organs differ according as the death is rapid or slow; if the death takes place within twenty-four hours, the effects are fairly uniform, the differences being only in degree; while, on the other hand, in those cases which terminate fatally from the more remote effects of the acid, there is some variety. It may be well to select two actual cases as types, the one patient dying from acute poisoning, the other surviving for a time, and then dying from ulceration and contraction of the digestive tract.

A hatter, early in the morning, swallowed a large mouthful of strong sulphuric acid, a preparation which he used in his work—(whether the draught was taken accidentally or suicidally was never known). He died within two hours. The whole tongue was sphacelated, parts of the mucous membrane being dissolved; the inner surface of the gullet, as well as the whole throat, was of a grey-black colour; the mucous membrane of the stomach was coal-black, and so softened that it gave way like blotting-paper under the forceps, the contents escaping into the cavity of the abdomen. The peritoneum was also blackened as if burnt; probably there had been perforation of the stomach during life; the mucous membrane of the duodenum was swollen, hardened, and looked as if it had been boiled; while the blood was of a cherry-red colour, and of the consistence of a thin syrup. The rest of the organs were healthy; chemical research on the fluid which had been collected from the stomach, gullet, and duodenum showed that it contained 87.25 grains of free sulphuric acid.*

This is, perhaps, the most extreme case of destruction on record; the cause of unusually violent action is referable to the acid acting on an empty stomach. It is important to note that even with this extensive destruction of the stomach, life was prolonged for two hours.

The case I have selected to serve as the type of a chronic but fatal illness produced from poisoning by sulphuric acid is one related by Oscar Wyss. A cook, thirty-four years of age, who had suffered many ailments, drank, on the 6th of November, 1867, by mistake, at eight o'clock in the morning, two mouthfuls of a mixture of 1 part of sulphuric acid and 4 of water. Pain in the stomach and neck, and vomiting of black masses, were the immediate symptoms, and two hours later he was admitted into the hospital in a state of collapse, with cold extremities, cyanosis of the face, &c. Copious draughts of milk were given, and the patient vomited much, the vomit still consisting of black

* Casper, vol. ii., case 194.

pultaceous matters, in which, on a microscopical examination, could be readily detected columnar epithelium of the stomach and mucous tissue elements. The urine was of specific gravity 1.033, non-albuminous; on analysis it contained 2.388 grms. of combined sulphuric acid.

On the second day there was some improvement in the symptom; the urine contained 1.276 grms. of combined sulphuric acid; on the third day 2.665 grms of combined sulphuric acid; and on the tenth day the patient vomited up a complete cast of the mucous membrane of the gullet. The patient remained in the hospital, and became gradually weaker from stricture of the gullet and impairment of the digestive powers, and died, two months after taking the poison on the 5th of January, 1868.

The stomach was found small, contracted, with many adhesions to the pancreas and liver; it was about 12 centimetres long (4.7 inch), and from 2-2.5 centimetres (.7 to .9 inch) broad, contracted to somewhat the form of a cat's intestine; there were several transverse rugae; the walls were thickened at the small curvature, measurements giving 5 mm. (.19 inch) in the middle, and beyond about 2.75 mm. (.11 inch); in the upper two-thirds, the lumen was so contracted as scarcely to admit the point of the little finger. The inner surface was covered with a layer of pus, with no trace of mucous tissue, and was everywhere pale-red, uneven, and crossed by cicatrical bands. In two parts, at the greater curvature, the mucous surface was strongly injected in a ring-like form, and in the middle of the ring was a deep funnel-shaped ulcer; a part of the rest of the stomach was strongly injected and scattered over with numerous punctiform, small, transparent bladders. The gullet was contracted at the upper part (just below the epiglottis) from 20-22 mm. (.78 to .86 inch) in diameter; it then gradually widened to measure about 12 mm. (.47 inch) at the diaphragm; in the neighbourhood of the last contraction the tissue was scarred, injected, and ulcerated; there were also small abscesses opening into this portion of the gullet.

The museums of the different London hospitals afford excellent material for the study of the effects of sulphuric acid on the pharynx, gullet, and stomach; and it may be a matter of convenience to students if the more typical examples at these different museums be noticed in detail, so that the preparations themselves may be referred to.

In St. Bartholomew's Museum, No. 1942, is an example of excessive destruction of the stomach by sulphuric acid. The stomach is much contracted, and has a large aperture with ragged edges; the mucous membrane is thickened, charged, and blackened.

No. 1,941, in the same museum, is the stomach of a person who died from a large dose of sulphuric acid. When recent, it is described as of a deep-red colour, mottled with black; appearances which, from long soaking in spirit, are

not true at the present time ; but the rough, shaggy state of the mucous tissue can be traced ; the gullet and the pylorus appear the least affected.

St. George's Hospital, ser., ix., 146, 11 and 43, e.—The pharynx and oesophagus of a man who was brought into the hospital in a state of collapse, after a large but unknown dose of sulphuric acid. The lips were much eroded, the mucous membrane of the stomach, pharynx, and oesophagus show an extraordinary shreddy condition ; the lining membrane of the stomach is much charred, and the action has extended to the duodenum ; the muscular coat is not affected.

Guy's Hospital, No. 1,799.—A preparation showing the mucous membrane of the stomach entirely denuded. The organ looks like a piece of thin paper.

No. 1,799²⁰.—The stomach of a woman who poisoned herself by drinking a wine-glassful of acid before breakfast. She lived eleven days. The main symptoms were vomiting and purging, but there was no complaint of pain. There is extensive destruction of mucous membrane along the lesser curvature and towards the pyloric extremity ; a portion of the mucous membrane is floating as a slough.

No. 1,799²¹ is the gullet and stomach of a man who took about three drachms of strong acid. He lived three days without much apparent suffering, and died unexpectedly. The lining membrane of the oesophagus has the longitudinal wrinkles or furrows so often, nay, almost constantly, met with in poisoning by the acids. The mucous tissue of the stomach is raised in cloudy ridges, and blackened.

No. 1,790²² is a wonderfully entire cast of the gullet from a woman who swallowed an ounce of sulphuric acid, and is said, according to the catalogue, to have recovered.

University College.—In this museum will be found an exquisite preparation of the effects of sulphuric acid. The mucous membrane of the oesophagus is divided into small quadrilateral areas by longitudinal and transverse furrows ; the stomach is very brown, and covered with shreddy and filamentous tissue ; the brown colour is without doubt the remains of extravasated and charred blood.

No. 6.201 is a wax case representing the stomach of a woman who died after taking a large dose of sulphuric acid. A yellow mass was found in the stomach ; there are two perforations, and the mucous membrane is entirely destroyed.

DETECTION AND ESTIMATION OF FREE SULPHURIC ACID.

The general method of separating the mineral acids is as follows : the tissues, or matters, are soaked in distilled water for some time. If no free acid is present, the liquid will not redden litmus paper, or give an acid reaction with any of the numerous tinctorial agents in use by the chemist for the purposes of titration. After sufficient digestion in water, the liquid extract is made up to some definite bulk and allowed to subside. Filtration is unnecessary. A small fractional part (say, for example, should the whole be 250 cc., $\frac{1}{100}$ th or 2.5 cc.) is taken, and using as an indicator cochineal or phenol-phthalein, the total acidity is estimated by a decinormal solution of soda. By this preliminary operation, some guide for the conduct of the future more exact operations is obtained. Should the liquid be very acid, a small quantity of the whole is

to be now taken, but if the acidity is feeble, a larger quantity is necessary, and sufficient quinine then added to fix the acid—100 parts of sulphuric acid are saturated by 342 parts of quinine monohydrate. Therefore, on the supposition that all the free acid is sulphuric, it will be found sufficient to add 3.5 parts of quinine for every 1 part of acid, estimated as sulphuric, found by the preliminary rough titration; and as it is inconvenient to deal with large quantities of alkaloid, a fractional portion of the liquid extract (representing not more than 50 mgrms. of acid) should be taken, which will require 175 mgrms. of quinine.

On addition of the quinine, the neutralised liquid is evaporated to dryness, or to approaching dryness, and then exhausted by strong alcohol. The alcoholic extract is, after filtration, dried up, and the quinine sulphate, nitrate, or hydrochlorate, as the case may be, filtered off and extracted by boiling water, and precipitated by ammonia, the end result being quinine hydrate (which may be filtered off and used again for similar purposes), and a sulphate, nitrate or chloride of ammonia in solution. It therefore remains to determine the nature and quantity of the acids now combined with ammonia. The solution is made up to a known bulk, and portions tested for chlorides by nitrate of silver, and for nitrates by the copper or the ferrous sulphate test. If sulphuric acid is present, there will be a precipitate of barium sulphate, which, on account of its density and insolubility in nitric or hydrochloric acids, is very characteristic. For estimating the sulphuric acid thus found, it will only be necessary to take a known bulk of the same liquid, heat it to boiling after acidifying by hydrochloric acid, and then add a sufficient quantity of baric chloride solution. Unless this exact process is followed, the analyst is likely to get a liquid which refuses to filter clear, but if the sulphate be precipitated from a hot liquid, it usually settles rapidly to the bottom of the vessel, and the supernatant fluid can be decanted clear, and the precipitate washed by decantation, and ultimately collected on a filter, dried, and weighed.

The sulphate of baryta found, multiplied by .3434, equals the sulphuric anhydride.

The older process was to dissolve the free sulphuric acid out by alcohol. As is well known, mineral sulphates are insoluble in, and are precipitated by, alcohol, whereas sulphuric acid enters into solution. The most valid objection, as a quantitative process, to the use of alcohol, is the tendency which all mineral acids have to unite with alcohol in organic combination, and thus, as it were, to disappear; and, indeed, results are found, by experiment, to be below the truth when alcohol is used. This objection does not hold good if either merely qualitative evidence, or a fairly approximate quantitation, is required. In such a case, the vomited matters, the contents of the stomach, or a watery

extract of the tissues, are evaporated to a syrup, and then extracted with strong alcohol and filtered ; a little phenol-phthalein solution is added, and the acid alcohol exactly neutralised by an alcoholic solution of clear decinormal or normal soda. According to the acidity of the liquid, the amount used of the decinormal or normal soda is noted, and then the whole evaporated to dryness, and finally heated to gentle redness. The alkaline sulphate is next dissolved in very dilute hydrochloric acid, and the solution precipitated by chloride of barium in the usual way. The quantitative results, although low, would, in the great majority of cases, answer the purpose sufficiently.

A test usually enumerated, Hilger's test for mineral acid, may be mentioned. A liquid which contains a very minute quantity of mineral acid, becomes of a blue colour (or, if 1 per cent. or above, of a green) * ; but this test, although useful in examining vinegars (see vol. i., p. 478), is not of much value in toxicology, and the quinine method for this purpose meets every conceivable case, both for qualitative and quantitative purposes.

The Urine.—Although an excess of sulphates is found constantly in the urine of persons who have taken large doses of sulphuric acid, the latter has never been found in that liquid in a free state, so that it will be useless to search for free acid. It is, therefore, only necessary to filter the fluid, and precipitate direct with an excess of chloride of barium. It is better to operate in this manner than to burn the urine to an ash, for in the latter case, part of the sulphates, in the presence of phosphates, are decomposed, and, on the other hand, any organic sulphur combinations are liable to be estimated as sulphates.

It may also be well to pass chlorine gas through the same urine which has been treated with chloride of barium, and from which the sulphate has been filtered off. The result of this treatment will be a second precipitate of sulphate derived from sulphur, in a different form of combination than that of sulphate.

The normal amount of sulphuric acid excreted daily, according to Thudichum, is from 1·5 to 2·5 grms., and organic sulphur up to 2 grm, in the twenty-four hours, but very much more has been excreted by healthy persons.

Lehmann made some observations on himself, and found that, on an animal diet, he excreted no less than 10·399 grms. of sulphuric acid per day, while on mixed food a little over 7 grms.; but as Thudichum justly observes, this great amount must be referred to individual peculiarity. The amount of sulphates has a decided relation to diet. Animal food, although not containing sulphates, yet, from the oxidation of the sulphur-holding albumen, produces a urine rich in sulphate. Thus

* On the addition of a solution of methyl aniline violet.

Vogel found that a person, whose daily average was 2.02 grms., yielded 7.3 on a meat diet. The internal use of sulphur, sulphides, and sulphates, given in an ordinary medicinal way, is traceable in the urine, increasing the sulphates. In chronic diseases the amount of sulphates is decreased, in acute increased.

Finally, it would appear that the determination of sulphates in the urine is not of much value, *save when the normal amount that the individual secretes is primarily known*. On the other hand, a low amount of sulphates in the urine of a person poisoned by sulphuric acid has not been observed, and one can imagine cases in which such a low result might have forensic importance.

The presence of albumen in the urine has been considered by some a constant result of sulphuric acid poisoning, but although when looked for it is usually found, it cannot be considered constant. O. Smoler,* in eighteen cases of various degrees of sulphuric acid poisoning, found nothing abnormal in the urine. Wyss† found in the later stages of a case indican and pus. E. Leyden and Ph. Munn ‡ always found blood in the urine, as well as albumen, with casts and cellular elements. Mannkopf § found albuminuria in three cases out of five; in two of the cases there were fibrinous casts; in two the albumen disappeared at the end of the second or third day, but in one it continued for more than twenty days. Bamberger || has observed an increased albuminuria, with separation of the colouring matter of the blood. In this case it was ascribed to the action of the acid on the blood.

The Blood.—In Casper's case, No. 193, the vena cava of a child, who died within an hour after swallowing a large dose of sulphuric acid, was filled with a cherry-red, strongly acid-reacting blood. Again, Casper's case, No. 200, is that of a young woman, aged 19, who died from a poisonous dose of sulphuric acid. At the autopsy, four days after death, the following peculiarities of the blood were thus noted:—“The blood had an acid reaction, was dark, and had (as is usual in these cases) a syrupy consistence, while the blood-corpuscles were quite unchanged. The blood was treated with an excess of absolute alcohol filtered, the filtrate concentrated on a water-bath, the residue exhausted with absolute alcohol, &c. It yielded a small quantity of sulphuric acid.”

Other similar cases might be noted, but it must not for a moment be supposed that the mass of the blood contains any free sulphuric acid

* *Archiv der Heilkunde red. v. E. Wagner*, 1869. Hft. 2, S. 181.

† *Wiener Medicinal-Halle*, 1861. Jahr. 6. No. 46.

‡ *Virchow's Archiv. f. Path. Anat.*, 1861. Bd. 22, Hft. 3 u. 4, S. 237.

§ *Wien Med. Wochenschrift*, 1862, Nro. 35. 1863, Nro. 5.

|| *Wien Med.-Halle*, 1864. Nro. 29, 30.

during life. The acidity of the blood in the *vena cava* may be ascribed to *post-mortem* endosmosis, the acid passing through the walls of the stomach into the large vessel.

Sulphates.—If the acid swallowed should have been entirely neutralised by antidotes, such as chalk, &c., it becomes of the first importance to ascertain, as far as possible, by means of a microscopical examination, the nature of the food remaining in the stomach, and then to calculate the probable contents in sulphates of the food thus known to be eaten. It will be found that with ordinary food, and under ordinary circumstances, only small percentages of combined sulphuric acid can be present.

As an example, take the ordinary rations of the soldier, viz.:—12 oz. of meat, 24 oz. of bread, 16 oz. of potatoes, 8 oz. of other vegetables; with sugar, salt, tea, coffee, and water. Now, if the whole quantity of these substances were eaten at a meal, they would not contain more than from 8 to 10 grains (5·6 grm.) of anhydrous sulphuric acid in the form of sulphates.

So far as the contents of the stomach are concerned, we have only to do with sulphates introduced in the food, but when once the food passes further along the intestinal canal, circumstances are altered, for we have sulphur-holding secretions, which, with ordinary chemical methods, yield sulphuric acid. Thus, even in the newly-born infant, according to the analysis of Zweifler, the mineral constituents of meconium are especially sulphate of lime, with a smaller quantity of sulphate of potash. The amount of bile which flows into the whole tract of the intestinal canal is estimated at about half a litre in the 24 hours; the amount of sulphur found in bile varies from 89 to 3 per cent., so that in 500 cc. we might, by oxidising the sulphur, obtain from 5 to 20 grms. of sulphuric anhydride.

It is therefore certain that large quantities of organic sulphur-compounds may be found in the human intestinal canal, for with individuals who suffer from constipation, the residues of the biliary secretion accumulate for many days. Hence, if the analyst searches for sulphates in excretal matters, all methods involving destruction of organic substances, whether by fire or by fluid-oxidising agents, are wrong in principle, and there is nothing left save to separate soluble sulphates by dialysis, or to precipitate direct out of an aqueous extract.

Again, sulphate of magnesia is a common medicine, and so is sodic sulphate; a possible medicinal dose of magnesia sulphate might amount to 56·7 grms. (2 oz.), the more usual dose being half that quantity. Lastly among the insane there are found patients who will eat plaster-of-Paris, earth, and similar matters, so that, in special cases, a very large amount of combined sulphuric acid may be found in the intestinal tract, without any relation to poisoning by the free acid; but in such instances

it must be rare, indeed, that surrounding circumstances or pathological evidence will not give a clue to the real state of affairs.

II.—HYDROCHLORIC ACID.

General Properties.—Hydrochloric acid, otherwise called *muriatic acid*, *spirit of salt*, is, in a strictly chemical sense, a pure gas, composed of 97.26 per cent. of chlorine, and 2.74 per cent. of hydrogen; but in an ordinary sense, it is a liquid, being a solution of the gas itself.

Hydrochloric acid is made on an enormous scale in the United Kingdom, the production being estimated at about a millions tons annually.

The toxicology of hydrochloric acid is modern, for we have no evidence that anything was known of it prior to the middle of the seventeenth century, when Glauber prepared it in solution, and, in 1772, Priestley, by treating common salt with sulphuric acid, isolated the pure gas.

The common liquid hydrochloric acid of commerce has a specific gravity of from 1.15 to 1.20, and contains usually less than 40 parts of hydrochloric acid in the 100 parts. The strength of pure samples of hydrochloric acid can be told by the specific gravity, and a very close approximation, in default of tables, may be obtained by simply multiplying the decimal figures of the specific gravity by 200. For example, an acid of 1.20 gravity would by this rule contain 40 per cent. of real acid, for $20 \times 200 = 40$.

The commercial acid is nearly always a little yellow, from the presence of iron derived from metallic retorts, and usually contains small quantities of chloride of arsenic,* derived from the sulphuric acid; but the colourless hydrochloric acid specially made for laboratory and medicinal use is nearly always pure.

The uses of the liquid acid are mainly in the production of chlorine, as a solvent for metals, and for medicinal and chemical purposes. Its properties are briefly as follows:—

It is a colourless or faintly-yellow acid liquid, the depth of colour depending on its purity, and especially its freedom from iron. The liquid is volatile, and can be separated from fixed matters and the less volatile acids by distillation; it has a strong attraction for water, and fumes when

* Some samples of hydrochloric acid have been found to contain as much as 4 per cent. of chloride of arsenic, but this is very unusual. Glenard found as a mean 2.5, As_2O_3 per kilogramme.

exposed to the air, from becoming saturated with aqueous vapour. If exposed to the vapour of ammonia, extremely dense clouds arise, due to the formation of the solid ammonium chloride. The acid boiled with a small quantity of manganese binoxide, evolves chlorine. Dioxide of lead has a similar action ; the chlorine may be detected by its bleaching action on a piece of paper dipped in indigo blue ; a little zinc-foil immersed in the acid disengages hydrogen. These two tests—viz., the production of chlorine by the one, and the production of hydrogen by the other—separate and reveal the constituent parts of the acid. Hydrochloric acid, in common with chlorides, give a dense precipitate with silver nitrate. The precipitate is insoluble in nitric acid, but soluble in ammonia ; it melts without decomposition. Exposed to the light, it becomes of a purple or blackish colour. Every 100 parts of silver chloride are equal to 25·43 of hydrochloric acid, HCl, and 63·5 parts of the liquid acid of specific gravity 1·20.

The properties of the pure hydrochloric acid gas are as follows :— Specific gravity, 1·262, consisting of equal volumes of hydrogen and chlorine, united without condensation. 100 cubic inches must therefore have a weight of 39·36 grains. The gas was liquefied by Faraday by means of a pressure of 40 atmospheres at 10° ; it was colourless and had a less refractive index than water.

Water absorbs the gas with avidity, 100 volumes of water absorbing 48,000 volumes of the gas, and becoming 143 volumes. The solution has all the properties of strong hydrochloric acid, specific gravity 1·21. The dilute hydrochloric acid of the Pharmacopœia should have a specific gravity of 1·052, and be equivalent to 10·58 per cent. of HCl.

Fatal Dose.—The dose which destroys life is not known with any accuracy. In two cases, adults have been killed by 14 grms. (half an ounce) of the commercial acid ; but, on the other hand, recovery is recorded, when more than double this quantity has been taken. A girl, fifteen years of age, died from drinking a teaspoonful of the acid.*

Amount of Free Acid in the Gastric Juice.—Hydrochloric acid exists in the gastric juice. This was first ascertained by Prout † in 1824 ; he separated it by distillation. The observation was afterwards confirmed by Gmelin, ‡ Children, § and Bracconnot. || On the other hand, Lehmann ¶

* *Brit. Med. Journ.*, March, 1871.

† “ *Philosophical Transactions*,” 1824, p. 45.

‡ P. Tiedmann and L. Gmelin, “ *Die Verdauung nach Versuchen.*” Heidelberg u. Leipsic, 1826, i.

§ “ *Annals of Philosophy*,” July, 1824.

|| *Ann. de Chim.*, t. lix., p. 348.

¶ *Journal f. Prakt. Chemie*, Bd. xl., 47.

pointed out that, as the stomach secretion contained, without a doubt, lactic acid, the act of distillation, in the presence of this lactic acid would set free hydrochloric acid from any alkaline chlorides. Blondlot and Cl. Bernard also showed that the gastric juice possessed no acid which would dissolve oxalate of lime, or develop hydrogen when treated with iron filings; hence there could not be free hydrochloric acid which even in a diluted state, would respond to both these tests. Then followed the researches of C. Schmidt,* who showed that the gastric secretion of men, of sheep, and of dogs contained more hydrochloric acid than would satisfy the bases present; and he propounded the view, now generally held, that the gastric juice does not contain absolutely free hydrochloric acid, but that it is in loose combination with the pepsin.

The amount of hydrochloric acid in the healthy stomach varies according as to whether digestion is actively proceeding or not, and entirely depends on the amount of gastric juice. Schmidt calculated it as 2 per cent. of the fresh juice. In diseased conditions, however, the amount may be greater, for Hoppe-Seyler † states that in 2·5 litres of gastric-juice from a patient with notable dilatation of the stomach, he found no lactic, but a large quantity of hydrochloric acid, so large, indeed, that, with moderate heating on the water bath, the acid was sufficiently concentrated to blacken the organic matters with which it was in contact.

Influence of Hydrochloric Acid on Vegetation.—Hydrochloric acid fumes, if emitted from works on a large scale, injure vegetation much. In former years, before any legal obligations were placed upon manufacturers, for the condensing of the volatile products, the nuisance from this cause was great. In 1823, the duty on salt being repealed by the government, an extraordinary impetus was given to the manufacture of hydrochloric acid, and since all the volatile products at that time escaped through short chimneys into the air, a considerable area of land round the works was rendered quite unfit for growing plants. The present law on the subject is, that the maximum quantity of acid escaping shall not exceed 2 grains per cubic foot of the air, smoke, or chimney gases; and according to the reports of Dr. Angus Smith, the condensation by the improved appliances is well within the Act, and about as perfect as can be devised.

It appears from the reports of the Belgian commission in 1855, when virtually no precautions were taken, that the gases are liable to injure vegetation to the extent of 2,000 metres (6,560) yards around any active works; the more watery vapour the air contains, the quicker is the gas precipitated and carried to the earth. If the action of the vapour is considerable, the leaves of plants dry and wither; the chlorophyll becomes

* Bidder u. Schmidt, *Verdaungs-Säfte, &c.*

† "Physiologische Chemie," von Dr. Felix Hoppe-Seyler, Theil ii., p. 220. Berlin, 1878.

modified, and no longer gives the normal spectrum, while a thickening of the rind of trees has also been noticed. The cereals suffer much ; they increase in stalk, but produce little grain. The leguminosæ become spotted, and have an air of dryness and want of vigour ; while the potato, among plants utilised for food, appears to have the strongest resistance. Vines are very sensitive to the gas. Among trees, the alder seems most sensitive ; then come fruit-trees, and last, the hardy forest-trees—the poplar, the ash, the lime, the elm, the maple, the birch, and the oak.*

Action upon Cloth and Manufactured Articles.—On black cloth the acid produces a green stain, which is not moist and shows no corrosion. On moist matters the stain is more or less reddish ; after a little time no free acid may be detected, by simply moistening the spot ; but if the stain is cut out and boiled with water, there may be some evidence of free acid. The absence of moisture and corrosion distinguishes the stain from that produced by sulphuric acid.

Poisonous Effects of Hydrochloric Acid Gas.—Eulenberg † has studied the effects of the vapour of this acid on rabbits and pigeons. One of these experiments may be cited in detail. Hydrochloric acid gas, prepared by heating together common salt and sulphuric acid, was passed into a glass shade supported on a plate, and a rabbit was placed in the transparent chamber thus formed. On the entrance of the vapour, there was immediate blinking of the eyes, rubbing of the paws against the nostrils, and emission of white fumes with the expired breath, while the respiration was irregular (40 to the minute). After the lapse of ten minutes, the gas was again introduced, until the atmosphere was quite thick ; the symptoms were similar to those detailed above, but more violent ; and in fourteen minutes from the commencement, the rabbit sank down on its right side (respiration 32). When twenty-two minutes had elapsed, the gas was again allowed to enter. The rabbit now lay quiet, with closed eyes and laboured respiration, and, finally, after half-an-hour of intermittent exposure to the gas, the animal was removed.

The cornea was opalescent, and the eyes filled with water ; there

* Those who desire to study more closely the effect of acids generally on vegetation may consult the various papers of the alkali inspectors contained in the Local Government Reports. See also Schubarth, *Die Sauerer Gase, welche Schwefelsäure und Soda-Fabriken verbreiten. Verhandlungen des Vereins zur Beförderung des Gewerbe-fleisses in Preussen*, 1857, S. 185. Dingler's *Journal*, Bd. 145, S. 374-427.

Christel, *Ueber die Einwirkung von Säuren-Dämpfen auf die Vegetation.*

Arch. f. Pharmacie, 1871, p. 252.

Vierteljahrsschrift für Gerichtliche Medicin, 17 Bd. S. 404, 1872.

† "Gewerbe Hygiène." Berlin, 1876, S. 51.

was frequent shaking of the head and working of the forepaws. After three minutes' exposure to the air, the respirations were found to be 128 per minute; this quickened respiration lasted for an hour, then gave place to a shorter and more superficial breathing. On the second day after the experiment, the rabbit suffered from laboured respiration (28 to the minute) and pain, and there was a rattling in the bronchial tubes. The animal died on the third day, death being preceded by slow respiration (12 to the minute).

The appearances twenty-four hours after death were as follows:—The eyes were coated with a thick slime, and both cornea were opalescent; there was strong rigidity of the body. The pia mater covering the brain was everywhere hyperæmic, and at the hinder border of both hemispheres appeared a small clot, surrounded by a thin layer of bloody fluid. The *plex. venos spin.* was filled with coagulated blood, and there was also a thin extravasation of blood covering the medulla and pons. The lungs were mottled bright brown-red; the middle lobe of the right lung was dark-brown, solid, and sank in water; the lower lobe of the same lung and the upper lobe of the left lung were nearly in a similar condition, but the edges were of a bright red. The parenchyma in the darker places on section did not crepitate. On the cut surface was a little dark, fluid, weakly-acid blood; the tracheal mucous membrane was injected. The heart was filled with thick coagulated blood; the liver was congested, of a reddish-brown colour, and rich in dark, fluid blood; in the *vena cava inferior* was coagulated blood. The kidneys were not hyperæmic; the intestines were superficially congested.

I think there can be little doubt that the symptoms during life, and the appearances after death, in this case are perfectly consistent with the following view:—The vapour acts first as a direct irritant, and is capable of exciting inflammation in the lung and bronchial tissues; but besides this, there is a secondary effect, only occurring when the gas is in sufficient quantity, and the action sufficiently prolonged—viz., a direct coagulation of the blood in certain points of the living vessels of the lungs. The consequence of this is a more or less general backward engorgement, the right side of the heart becomes distended with blood, and the ultimate cause of death is partly mechanical. The hyperæmia of the brain membranes, and even the haemorrhages, are quite consistent with this view, and occur in cases where the obstruction to the circulation is of a coarser and more obvious character, and can therefore be better appreciated.

Effects of the Liquid Acid.—There is one distinction between poisoning by hydrochloric and the other mineral acids—namely, the absence of corrosion of the skin. Ad. Lesser* has established by direct

* *Virchow's Archiv f. Path. Anat.*, Bd. 83, Hft. 2, S. 215, 1881.

experiment, that it is not possible to make any permanent mark on the skin by the application even of the strongest commercial acid (40 per cent.). Hence, in any case of suspected poisoning by acid, should there be stains on the lips and face as from an acid, the presumption will be rather against hydrochloric. The symptoms themselves differ very little from those produced by sulphuric acid. The pathological appearances also are not essentially different, but hydrochloric is a weaker acid, and the extensive disorganisation, solution, and perforation of the viscera, noticed occasionally with sulphuric acid, have never been found in hydrochloric acid poisoning. We may quote here the following case:—

A woman, under the influence of great and sudden grief—not unmixed with passion—drew a bottle from her pocket, and emptied it very quickly. She immediately uttered a cry, writhed and vomited a yellow-green fluid. The abdomen also became enlarged. Milk was given her, but she could not swallow it, and death took place, in convulsions, two hours after the drinking of the poison.

The *post-mortem* appearances were briefly as follows:—Mouth and tongue free from textural change; much gas in the abdomen, more especially in the stomach; the membranes of the brain congested; the lungs filled with blood. The stomach was strongly pressed forward, of a dark brown-red, and exhibiting many irregular blackish spots, varying from two lines to half-an-inch in diameter (the spots were drier and harder than the rest of the stomach); the mucous membrane, internally, was generally blackened, and changed to a carbonised, shaggy, slimy mass, while the organ was filled with a blackish homogeneous pulp, which had no odour. The gullet was also blackened. A considerable quantity of hydrochloric acid was separated from the stomach.*

The termination in this instance was unusually rapid. In a case detailed by Casper,† in which a boy drank an unknown quantity of acid, death took place in seven hours. In Guy's Hospital museum, the duodenum and stomach are preserved of a patient who is said to have died in nine and a half hours from half an ounce of the acid. The same quantity, in a case related by Taylor, caused death in eighteen hours. From these and other instances, it may be presumed that death from acute poisoning by hydrochloric acid will probably take place within twenty-four hours.

Post-mortem Appearances.—The pathological appearances are very similar to those found in the case already detailed; though the skin of

* *Preuss. Med. Vereinszeit. u. Friederichs Blätter f. Gerichtl. Anthropologie*, 1858, Hft. 6, S. 70.

† Case 230.—*Gerichtliche Medicin*, 6th Ed., Berlin, 1876

the face may not be eroded in any way by the acid, yet the more delicate mucous membrane of the mouth, gullet, &c., appears to have been always changed, and is usually white or whitish-brown. Perforation of the stomach has not been noticed.

In Guy's Hospital museum (prep. 1,799¹⁶), the stomach and duodenum of the case mentioned exhibit the mucous membrane considerably injected, with extravasations of blood, which, at the time when the preparation was first arranged, were of various tints, but are now somewhat altered, through long keeping in spirit. In St. George's Hospital museum (ser. ix., 43, d. 200) are preserved the stomach and part of the duodenum of a person, who died from hydrochloric acid. The case is detailed in the *Medical Times and Gazette* for 1853, vol. ii., p. 513. The whole inner surface appears to be in a sloughing state, and the larynx and lung were also inflamed.

A preparation, presented by Mr. Bowman to King's College Hospital museum, exhibits the effects of a very large dose of hydrochloric acid. The gullet has a shrivelled and worm-eaten appearance; the stomach is injected with black blood, and was filled with an acid, grumous matter.*

Looking at these and other museum preparations illustrating the effects of sulphuric and hydrochloric acids, I was unable (in default of the history of the cases) to distinguish between the two, by the naked eye appearances, save in those cases in which the disorganisation was so excessive as to render hydrochloric acid improbable. On the other hand, the changes produced by nitric acid are so distinctive, that it is impossible to mistake its action for that of any other acid. The nitric acid pathological preparations may be picked out at a glance.

Detection and Estimation of Free Hydrochloric Acid.—The detection of free hydrochloric acid presents no difficulty. The contents of the stomach (or a watery extract of the latter) are distilled, and the distillate precipitated with silver nitrate solution. It is perfectly true that a healthy stomach thus treated will yield a distillate giving a faint cloud with silver nitrate; but if any percentage of free acid is in the stomach, as in cases of poisoning, there is an abundant precipitate, which may be collected and weighed in the usual manner. It may also be urged that if free sulphuric acid is present, or if there is free lactic acid, chlorides by distillation may be broken up and yield hydrochloric acid. This is certainly the case, but anyone engaged in practical work would naturally test for sulphuric acid; and it is always open, where there is doubt, to extract the free mineral acids by quinine, as recommended in the article on sulphuric acid (page 67).

The only silver precipitates insoluble in nitric acid, when the acid

* A drawing of parts of the gullet and stomach is given in Guy and Ferrier's "Forensic Medicine."

contents of the stomach are distilled, are cyanide or chloride of silver. The properties of cyanide of silver are quite different from those of chloride (see the article on the cyanides), and the history of the case would probably be widely different. On the other hand, I have several times met with a distillate from the stomach, when neutral, giving a fair precipitate with nitrate of silver, but immediately dissolving on the addition of a drop of nitric acid. For exact quantitative results, it will be necessary to distill to dryness. This operation, in the presence of much organic matter, is best conducted in the perfect vacuum of the mercury pump (see fig. 8, p. 51); the receiver should contain a known quantity of normal soda solution, and be surrounded with ice. The chlorine in the distillate may be estimated volumetrically by the aid of a volumetric solution of nitrate of silver, using as an indicator neutral chromate of potash. (See vol. i., "Analysis of Foods," p. 516).

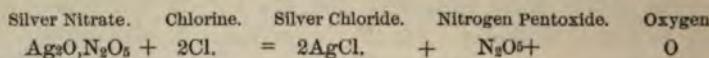
In investigating the stains from hydrochloric acid on fabrics, or the leaves of plants, any free hydrochloric acid may be separated by boiling with water, and then investigating the aqueous extract. Should, however, the stain be old, all free acid may have disappeared, and yet some of the chlorine remain in organic combination with the tissue, or in combination with bases. Dr. Angus Smith has found weighed portions of leaves, etc., which had been exposed to the action of hydrochloric acid fumes, richer in chlorides than similar parts of the plants not thus exposed.

The most accurate method of investigation is to cut out the stained portions, weigh them, and burn them up in a combustion-tube, the front portion of the tube being filled with caustic lime known to be free from chlorides; a similar experiment must be made with the unstained portions. In this way a considerable difference may often be found; and it is not impossible, in some instances, to thus detect, after the lapse of many years, that certain stains have been produced by a chlorine-holding substance.

III.—NITRIC ACID.

Nitric acid, commonly known in England as *aqua fortis*, chemically as *nitric acid*, *hydric nitrate*, or *nitric mono-hydrate*—is a mono-hydrate of nitrogen pentoxide, (N_2O_5). Two equivalents, or 126 parts of nitric acid containing 108 of N_2O_5 and 18 of H_2O anhydrous nitric acid, or nitrogen pentoxide, can be obtained by passing, with special precautions,

dry chlorine over silver nitrate. The products are free oxygen and nitrogen pentoxide, according to the following equation :—



By surrounding the receiver with a freezing mixture, the acid is condensed in crystals, which dissolve in water, with emission of much heat, forming nitric acid. Sometimes the crystals, though kept in sealed tubes, decompose, and the tube, from the pressure of the liberated gases bursts with a dangerous explosion.

Properties.—Pure nitric acid has a specific gravity of 1.52, and boils at 98°. Dr. Ure examined the boiling point and other properties of nitric acid very fully. An acid of 1.5 gravity boils at 98.8°; of specific gravity 1.45, at 115.5°; specific gravity 1.40, at 118.8°; of specific gravity 1.42, at 122.8°. The acid of specific gravity of 1.42 is the standard acid of the British Pharmacopœia. It can always be obtained by distilling either strong or moderately weak nitric acid; for, on the one hand, the acid on distillation gets weaker until the gravity of 1.42 is reached, or, on the other, it becomes stronger.

There is little doubt that acid of 1.42 gravity is a definite hydrate, consisting of one atom of dry acid and 4 atoms of water; it corresponds to 75 per cent.* of the liquid acid HNO_3 . There are also at least two other hydrates known—one an acid of 1.485 specific gravity, corresponding to 1 atom of dry acid and 2 of water, and an acid of specific gravity 1.334, corresponding to 1 atom of dry acid and 7 atoms of water.

In Germany the officinal acid is of 1.185 specific gravity, corresponding to about 30 per cent. of HNO_3 . The dilute nitric acid of the Pharmacopœia is a colourless liquid, of specific gravity 1.101, and should contain about 19 per cent. of acid. The acids used in various industries are known respectively as *dyers'* and *engravers'* acids. *Dyers'* acid has a gravity of 1.33 to 1.34 (66° to 68° Twad.), that is, strength from 56 to 58 per cent. of HNO_3 . *Engravers'* acid is stronger; being of 1.40 specific gravity (80° Twad.); and contains 70 per cent. of HNO_3 . Although the *pure* acid of commerce is (and should be) almost colourless, most commercial specimens are of hues from yellow up to deep-red. An acid saturated with red oxides of nitrogen is often known as “fuming nitric acid.”

Use in the Arts.—Nitric acid is employed very extensively in the arts and manufactures. The dyer uses it as a solvent for tin in the preparation of valuable mordaunts for calico and other fabrics; the engraver uses it for etching copper. It is an indispensable agent in the manufac-

* The British Pharmacopœia states that the 1.42 acid equals 70 per cent. of HNO_3 ; but this is not in accordance with Ure's Tables, nor with the facts.

ure of gun-cotton, nitro-glycerine, picric-acid, and sulphuric acid ; it is also used in the manufacture of tallow, in preparing the felt for hats, and in the gilding trades. It is said to be utilised to make yellowish orawn-coloured spots on cigar leaves, so as to give them the appearance of ge and quality. It is also used as a medicine.

Fatal Dose.—The dose which causes death has not been ascertained with any exactness. As in the case of sulphuric acid, we may go so far as to say that it is possible for a few drops of the strong acid to be fatal, or if brought into contact with the vocal apparatus, fatal spasm of the lottis might be excited. The smallest dose on record is 7.7 grms. (2 rachms), which killed a child aged 13.

Action of Nitric Acid on Vegetation.—Nitric acid acts on plants injuriously in a two-fold manner—viz., by direct corrosive action, and also by decomposing the chlorides which all plants contain, thus setting free chlorine, which decomposes and bleaches the chlorophyll. The action is most intense on soft and delicate leaves, such as those of clover, the cabbage, and all the cruciferæ. The tobacco plant is particularly injured by nitric acid. Next to all herbaceous plants, trees, such as the apple, pear, and fruit trees, generally suffer. The coniferae, whether from their impregnation with resin, or from some other cause, possess a considerable resisting power against nitric acid vapour, and the same is true as regards the cereals ; in the latter case, their siliceous armour acts as a preserving agent.

Nitric Acid Vapour.—The action of nitric acid in a state of vapour, as evolved by warming potassic nitrate and sulphuric acid together, has been studied by Eulenberg. A rabbit was placed under a shade into which 3 grains of nitric acid in a state of vapour were introduced. From the conditions of the experiment, some nitric peroxide must also have been present. Irritation of the external mucous membranes and embarrassment in breathing were observed. The animal in forty-five minutes was removed, and suffered afterwards from a croupous bronchitis, from which, however, it completely recovered in eleven days. A second experiment with the same animal was followed by death. On inspection, there was found strong injection of the cerebral membranes, with small extravasations of blood ; the lungs were excessively congested ; the right middle lobe especially was of a liver-brown colour, and empty of air : it sank in water.

O. Lassar* has also made a series of researches on the influence of nitric acid vapour, from which he concludes that the acid is not absorbed by the blood, but acts only by its mechanical irritation, for he could not trace, by means of an examination of the urine, any evidence of such absorption.

* Hoppe-Seyler's *Zeitschrift f. Physiol. Chemie.*, Bd. i., S. 165-173, 1877-78.

There are a few instances on record of the vapour having been fatal to men; for example, the well-known case of Mr. Haywood, a chemist of Sheffield, may be cited. In pouring a mixture of nitric and sulphuric acids from a carboy of sixty pounds' capacity, the vessel broke, and for a few minutes he inhaled the mixed fumes. He died eleven hours after the accident, although for the first three hours there were scarcely any symptoms of an injurious effect having been produced. On inspection, there was found intense congestion of the windpipe and bronchial tubes, with effusion of blood in the latter. The lining membrane of the heart and aorta was inflamed; unfortunately, the larynx was not examined.*

A very similar case happened in Edinburgh in 1864.† Two young men were carrying a jar of nitric acid; the jar broke, and they attempted to wipe up the acid from the floor. The one died ten hours after the accident, the other in less than twenty-four hours. The symptoms were mainly those of difficult breathing, and it is probable that death was produced from suffocation. Dr. Taylor relates also, that having accidentally inhaled the vapour in preparing gun-cotton, he suffered from severe constriction of the throat, tightness in the chest, and cough, for more than a week.‡

Effects of Liquid Nitric Acid.—Poisoning by nitric acid, though still rare, is naturally more frequent than formerly. At the beginning of this century, Tartra § wrote a most excellent monograph on the subject, and collated all the cases he could find, from the first recorded instances related by Bembo || in Venetian history, down to his own time. The number of deaths in those 400 years was but 55, while, in our century, at least 50 can be numbered. Most of these (74 per cent.) are suicidal, a very few homicidal, the rest accidental. In one of Tartra's cases, some nitric acid was placed in the wine of a drunken woman, with fatal effect. Osenbrüggen ¶ relates the case of a father murdering his six children by means of nitric acid; and C. A. Buchner ** that of a soldier who poured acid into the mouth of his illegitimate infant. A curious case is one

* *Lancet*, April 15, 1854, p. 430.

† *Chemical News*, March 14, 1863, p. 132.

‡ "Principles and Practice of Medical Jurisprudence," vol. i., 1873, p. 218.

§ Tartra, A. E. Dr., *Traité de l'Empoisonnement par l'Acide Nitrique*. Paris, An. 10 (1802), pp. 300.

|| *Bembo Cardinalis, Rerum Venetiarum Historiæ*, lib. xii., lib. i., p. 12, Paris Ed., 1551.

¶ *Allgem-Deutsche Strafrechtszeitung*, herausgeg. v. Frz. v. Holtzendorff. 5 Jahrg., 1865, Hft. 5, S. 273.

** Friederich's *Blätter f. Ger. Med.*, 1866, Hft. 3, S. 187.

in which a man poisoned his drunken wife by pouring the acid into her right ear ; she died after six weeks' illness. All these instances prove again, if necessary, that the acid is only likely to be used with murderous intent in the case of young children, or of sleeping, drunken, or otherwise helpless people.

As an example of the way in which accidents are brought about by heedlessness, may be cited the recent case of a woman who bought a small quantity of aqua fortis for the purpose of allaying toothache by a local application. She attempted to pour the acid direct from the bottle into the cavity of the tooth ; the acid went down her throat, and the usual symptoms followed. She threw up a very perfect cast of the gullet (preserved in University College museum), and rapidly died. Nitric acid has been mistaken for various liquids, and has also been used by injection as an abortive, in every respect having a toxicological history similar to that of sulphuric acid.

Local Action.—When strong nitric acid comes in contact with organic matters, there is almost constantly a development of gas. The tissue is first bleached, and then becomes of a more or less intense yellow colour. Nitric acid spots on the skin are not removed by ammonia, but become of an orange-red when moistened with potash and a solution of cyanide of potash. The yellow colour seems to show that picric acid is one of the constant products of the reaction ; sulphide of ammonium forms a sort of soap with the epidermis thus attacked, and detaches it.

Symptoms.—The symptoms and course of nitric acid poisoning differ in a few details only from those of sulphuric acid. There is the same instant pain and frequent vomiting, destruction of the mucous membranes, and, in the less severe cases, after-contraction of the gullet, &c.

One of the differences in the action of nitric and sulphuric acids is the constant development of gas with the former. This, without doubt, adds to the suffering. Tartra made several experiments on dead bodies, and showed that very considerable distention of the intestinal canal, by gaseous products, was the constant result ; the tissues were corroded and almost dissolved, being transformed, ultimately, into a sort of greasy paste. The vomited matters are of a yellow colour, unless mixed with blood, when they are of a dirty-brown hue, with shreds of yellow mucous, and have the strong acid reaction and smell of nitric acid. The teeth may be partially attacked from the solvent action of the acid on the enamel. The fauces and tongue, at first blanched, soon acquire a citron-yellow, or even a brown colour ; the whole cavity may swell and inflame, rendering the swallowing of liquids difficult, painful, and sometimes impossible. The air passages may also become affected, and in one case tracheotomy was performed for the relief of the breathing.* The stomach

* Arnott, *Med. Gaz.* vol. xii., p. 220.

rejects all remedies; there are symptoms of collapse; quick, weak pulse, frequent shivering, obstinate constipation, and death (often preceded by a kind of stupor), in from eighteen to twenty-four hours. The intellectual faculties remain clear, save in a few rare instances.

C. A. Wunderlich has recorded an unusual case, in which the symptoms were those of dysentery, and the large intestine was found acutely inflamed, while the small one was little affected. The kidneys had the same appearance as in Bright's disease.* The smallest fatal dose given by Taylor is from two drachms, which killed a child aged 13 years. Should the dose of nitric acid be insufficient to kill at once, or, what amounts to the same thing, should the acid be immediately diluted with water, or in some way be neutralized, the patient, as in the case of sulphuric acid, may yet die at a variable future time from stenosis of the gullet, impaired digestion, &c. For example, in an interesting case related by Tartra,† a woman, who had swallowed 42 grms. (1.5 oz.) of nitric acid, feeling acute pain, took immediately a quantity of water, and three hours afterwards was admitted into hospital, where she received appropriate treatment. At the end of a month she left, believing herself cured; but in a little while returned, and was re-admitted, suffering from marasmus, extreme weakness, and constant vomiting; ultimately she died. The *post-mortem* examination revealed extreme contraction of the intestinal canal throughout. The lumen would hardly admit a penholder. The stomach was no larger than an ordinary intestine, and adherent to adjacent organs; on its internal surface there were spots, probably cicatrices; there were also changes in the gullet, but not so marked. A somewhat similar case is related by the same author in his thirteenth observation.

Post-mortem Appearances.—The pathological changes in the tongue, gullet, and stomach can be readily studied from the preparations in the different museums. The staining by the nitric acid appears unchanged to the naked eye for many years; hence, most of the nitric acid preparations are in an excellent state of preservation. A very good example of the pathological changes is to be found in Nos. 1049 and 1050, University College museum.

No. 1049 presents the tongue, pharynx, and larynx of a man who had swallowed a teacupful of nitric acid. The epithelium of the oesophagus is for the most part wanting, and hangs in shreds; the dorsum of the tongue, in front of the circumvallate papillæ, is excavated, and over its central part superficially ulcerated; in other places the tongue is encrusted with a thick, loose, fawn-coloured layer, formed probably of des-

* *De Actionibus quibusdam Acidi Nitrici Caustico in Corpus Humanum immisiti. Programma Academ. Lipsiae, 1857, 4.*

† *Op. cit.*

quamated epithelium. The whole of the mucous surface is stained of a dirty yellow.

No. 1,050 is a preparation showing the tongue, gullet, and stomach of a person who died from the effects of nitric acid. The tongue in places is smooth and glazed ; in others, slightly depressed and excavated. On the anterior wall and lower portion of the gullet two large sloughs exist.

Although perforation of the stomach is not so common with nitric as with sulphuric acid, such an accident may occur, as shown in a preparation at Guy's Hospital, in which there is a perforation at the cardiac end. All the mucous membrane has disappeared, and the inner surface is for the most part covered with flocculent shreds. Three ounces of nitric acid are said to have been swallowed, and the patient lived seventeen hours. There is the usual staining.

In St. Bartholomew's museum, there is a very good specimen (No. 1,870) of the appearances in the gullet and stomach after poisoning by nitric acid. The case is detailed in St. Bartholomew's Hospital reports, vol. v., p. 247. A male died in fifteen hours after swallowing one ounce of nitric acid. The whole mucous membrane is wrinkled, or rather ploughed, into longitudinal furrows ; the yellow discolouration stops abruptly, with an irregular border, at the commencement of the stomach, the epithelial and mucous coats of which are wanting—its surface being rough and of a brownish-red colour.

The following preparations are to be found in the museum of the London Hospital :—A. c. 1. and A. b. 8.—A. c. 1. shows the pharynx, oesophagus, larynx, and stomach of a young woman, who, after taking half an ounce of nitric acid, died in eight hours. The staining is very intense ; as an unusual feature it may be noted that the larynx is almost as yellow as the oesophagus. The abrasion or solution of the epithelium on the dorsum of the tongue has dissected out the circumvallate and fungiform papillae, so that they project with unusual distinctness. The lining membrane of the gullet throughout is divided into minute squares by longitudinal and transverse furrows. The mucous membrane of the stomach appears wholly destroyed, and presents a woolly appearance.

A. b. 8. shows a very perfect cast of the oesophagus. The case was that of a woman, aged 35, who swallowed half an ounce of nitric acid. The symptoms for the first four days were the usual pain in the throat and stomach, which might be expected ; the bowels were freely open, and the stools dark and offensive. On the sixth day, there was constant vomiting with offensive breath ; on the ninth, the appearance of the patient was critical, and she threw up the cast preserved. She died on the tenth day after the taking of the acid. The gullet, stomach, trachea, and larynx were found after death much inflamed.

The following preparations are in St. Thomas' Hospital :—P. 5.—a stomach with gullet attached. The stomach is covered with yellowish-green patches of false membrane and deposit ; the gullet has the usual longitudinal furrows so characteristic of corrosive fluids.

P. 6. is also from a case of nitric acid poisoning. It shows the lining membrane of the stomach partly destroyed and shreddy, yet but little discolored, the hue being a sort of delicate fawn.

Detection and Estimation of Nitric Acid.—The detection either of free nitric acid or of its salts is not difficult. Free nitric acid, after preliminary estimation of the total acidity by decinormal soda, may be separated by the quinine process given at page 66. On precipitation of the quinine by ammonia or soda solution, the nitrate of ammonia or soda (and, it may be, other similarly combined acids) remain in solution. If free nitric acid is present in small quantity only, it may be necessary to evaporate the filtrate from the quinine nearly to dryness, and to test the concentrated liquid for nitric acid. The ordinary tests are as follows :—

(1.) Nitrates, treated with mercury or copper and strong sulphuric acid, develop nitric oxide, recognised by red fumes, if mixed with air or oxygen.

(2.) A nitrate dissolved in a small quantity of water, with the addition of a crystal of ferrous sulphate (allowed to partially dissolve), and then of strong sulphuric acid—poured through a funnel with a long tube dipping to the bottom of the test tube, so as to form a layer at the bottom—strikes a brown colour at the junction of the liquid. When the test is properly performed, there will be three layers—the uppermost being the nitrate solution, the middle ferrous sulphate, and the lowest sulphuric acid ; the middle layer becomes of a smoky or black hue, if a nitrate is present. Organic matter interferes much with the reaction.

(3.) Nitrates in solution, treated in the cold with a zinc copper couple, are decomposed first into nitrites, and then into ammonia. The nitrites may be detected by a solution of meta-phenyldiamine, which strikes a red colour with an infinitesimal quantity. Hence a solution which gives no red colour with meta-phenyldiamine, when submitted to the action of a zinc copper couple, and tested from time to time, cannot contain nitrites ; therefore no nitrates were originally present.

(4) Nitrates, on being treated with strong sulphuric acid, and then a solution of indigo-carmine dropped in, as described in vol. i. "Foods," p. 521, is also a very useful test—not conclusive in itself, but readily applied, and if the quinine method of separation has been resorted to, with few sources of error.

There is a process of separating nitric acid direct from any organic tissue, which may sometimes be useful :—Place the substance in a strong,

wide-mouthed flask, closed by a caoutchouc cork, and in the flask put a small, short test-tube, charged with a strong solution of ferrous chloride in hydrochloric acid. The flask is connected to the mercury pump (fig. 8, p. 51), and made perfectly vacuous by raising and lowering the reservoir. When this is effected, the tube SS'P is adjusted so as deliver any gas evolved into a eudiometer, or other gas-measuring apparatus. By a suitable movement of the flask, the acid ferrous chloride is allowed to come in contact with the tissue, a gentle heat applied to the flask, and gases are evolved. These may be carbon dioxide, nitrogen, and nitric oxide. On the evolution of gas ceasing, the carbon dioxide is absorbed by passing up under the mercury a little caustic potash. When absorption is complete, the gas, consisting of nitrogen and nitric oxide, may be measured. A bubble or two of oxygen is now passed into the eudiometer; if nitric oxide is present, red fumes at once develop. On absorbing the excess of oxygen and the nitric peroxide by alkaline pyrogallate, and measuring the residual gas, it is easy to calculate how much nitric oxide was originally present, according to the principles laid down in vol. i. of the present work, p. 533.

It is also obvious that, by treating nitric oxide with oxygen, and absorbing the nitric peroxide present by an alkaline liquid of known strength and free from nitrates of ammonia, the resulting solution may be dealt with by a zinc copper couple, and the ammonia developed by the action of the couple directly estimated by titration by a decinormal hydrochloric acid, if large in quantity, or by "*nesslerising*," if small in quantity. Crum's method of estimating nitrates (vol. i., p. 520) in the cases of minute stains on fabrics, &c., with a little modification, may be occasionally applicable.

IV.—AMMONIA.

Ammonia (NH_3) is met with either as a vapour or gas, or as a solution of the pure gas in water; the gas may also be found as a liquid.

Properties.—Pure ammonia gas is colourless, with a strong, irritating, pungent odour, forming white fumes of ammonic chloride, if exposed to hydric chloride vapour, and turning red moist litmus paper strongly blue. By intense cold, or by a pressure of $6\frac{1}{2}$ atmospheres at the ordinary temperature, the gas is readily liquefied; the liquid ammonia boils at 38° ; its observed specific gravity is $.731$; it freezes at -57.1° . Ammonia is readily absorbed by water; at 0° water will take up 1,000 times its own volume, and at ordinary temperatures about 600 times its

volume. Alcohol also absorbs about 10 per cent. Ammonia is a strong base, and forms a number of salts. Ammonia is one of the constant products of the putrefaction of nitrogenous substances; it exists in the atmosphere in small proportions, and in everything that contains water. Indeed, water is the only compound equal to it in its universality of diffusion. The minute quantities of ammonia thus diffused throughout nature are probably never in the free state, but combinations of ammonia with hydric nitrate, carbon dioxide, &c.

*Uses.**—A solution of ammonia in water has many applications in the arts and industries; it is used in medicine, and is an indispensable laboratory reagent.

The officinal caustic preparations of ammonia are—*ammoniæ liquor fortior* (*strong solution of ammonia*), which should contain 32.5 per cent. of ammonia, and have a specific gravity of .891.

Liquor ammoniæ (*solution of ammonia*), specific gravity .959, and containing 10 per cent. of ammonia. There is also a *liniment of ammonia*, composed of olive-oil 3 parts, and ammonia 1 part.

Strong solution of ammonia is an important ingredient in the “*linimentum camphoræ composita* (*compound liniment of camphor*), the composition of which is as follows: camphor, 2.5 parts; oil of lavender, .125; strong solution of ammonia, 5.0; and rectified spirit, 15 parts. Its content of strong solution of ammonia is then about 22.6 per cent. (equivalent to 7.3 of NH_3).†

The Carbonate of Ammonia is also caustic; its formula is probably $(\text{NH}_4)_2\text{CO}_3 + 2(\text{NH}_4\text{HCO}_3) + 2\text{H}_2\text{O}$. It is in the form of colourless, crystalline masses; the odour is powerfully ammoniacal; it is strongly alkaline, and the taste is acrid. It completely volatilises with heat, is soluble in water, and somewhat soluble in spirit.

The officinal preparation is the “*spiritus ammoniæ aromaticus*,” or aromatic spirit of ammonia. It is made by distilling ammonic carbonate, 8 parts; strong solution of ammonia, 4 parts; rectified spirit, 120 parts; water, 60 parts; volatile oil of nutmeg, 5 parts; and oil of lemon, .75 part. The distillation is stopped when 140 parts have distilled over; it hence follows that the aromatic spirit of ammonia is a solution of neutral carbonate, flavoured with oil of lemon and nutmeg in a weak spirit.

* Dr. W. B. Richardson has shown that ammonia possesses powerful anti-septic properties.—*Brit. Med. Journal*, 1862.

† There is a common liniment for horses used in stables, and popularly known as “white-oil.” It contains 1 part of ammonia and 4 parts of olive or rape-oil; not unfrequently turpentine is added. Another veterinary liniment, called “egg-oil,” contains ammonia, oil of origanum, turpentine and the yolks of eggs.

Smelling Salts (sal volatile) are composed of carbonate of ammonia.

Statistics.—Falck has found throughout literature, notices of thirty cases of poisoning by ammonia, or some of its preparations. In two of these it was used as a poison for the purpose of murder, and in eight with suicidal intent; the remainder were all accidental. The two criminal cases were those of children, who both died. Six out of eight of the suicidal, and twelve of the twenty accidental cases, also terminated fatally. Ammonia occupies, in order of frequency, about the thirteenth place of all poisons in England at the present time.

Poisoning by Ammonia Vapour.—Strong ammoniacal vapour is fatal to both animal and vegetable life. There are, however, but few instances of poisoning by ammonia vapour, and the few cases which have occurred have been, without exception, the result of accident. Two cases of death are recorded, due to an attempt to rouse epileptics from stupor, by an injudicious use of strong ammonia applied to the nostrils. In another case, when hydrocyanic acid had been taken, there was the same result. An instance is also on record of poisonous effects from the breaking of a bottle of ammonia, and the sudden evolution in this way of an enormous volume of the caustic gas. Lastly, a man employed in the manufacture of ice, by means of the liquefaction of ammonia (Carré's process), breathed the vapour, and had a narrow escape for his life.

Symptoms.—The symptoms observed in the last case may well serve as a type of what may be expected to occur after breathing ammonia vapour. The man remained from five to ten minutes in the stream of gas; he then experienced a feeling of anxiety, and a sense of constriction in the epigastrium, burning in the throat, and giddiness. He vomited. The pulse was small and frequent, the face pale, the mouth and throat strongly reddened, with increased secretion. Auscultation and percussion of the chest elicited nothing abnormal, although during the course of four days he had from time to time symptoms of suffocation, which were relieved by emetics. He recovered by the eighth day.*

In experiments on animals, very similar symptoms are produced. There is increased secretion of the eyes, nose, and mouth, with redness. The cry of cats becomes remarkably hoarse, and they generally vomit. Great difficulty in breathing and tetanic convulsions are present. When the animal is confined in a small closed chamber, death takes place in about a quarter of an hour.

On section, the bronchial tubes, to the finest ramifications, are found to be filled with a tenacious mucous, and the air passages, from the glottis throughout, reddened. The lungs are emphysematous, but have not always any special colour; the heart contains but little coagulated blood; the blood has a dark-red colour.

* Schmidt's *Jahrbuch*, 1872, i., S. 30.

The chronic effects of the gas, as shown in workmen engaged in manufactures in which the fumes of ammonia are frequent, appear to be an inflammation of the eyes and an affection of the skin. The latter is thought to be due to the ammonia uniting to form a soap with the oil of the lubricating skin glands. Some observers have also noticed deafness, and a peculiar colour of the skin of the nose and forehead, among those who work in guano factories. Its usual action on the body appears to be a diminution of the healthy oxidation changes, and a general lowering of bodily strength, with evident anaemia.

Ammonia in Solution.—Action on Plants.—Solutions of strong ammonia, or solutions of the carbonate, act injuriously on vegetable life, while the neutral salts of ammonia are, on the contrary, excellent manures. A 30 per cent. solution of ammonic carbonate kills most plants within an hour, and it is indifferent whether the whole plant is watered with this solution, or whether it is applied only to the leaves. If, after this watering of the plant with ammonic carbonate water, the injurious salt is washed out as far as possible by distilled water, or by a weakly acidulated fluid, then the plant may recover, after having shed more or less of its leaves. These facts sufficiently explain the injurious effects noticed when urine is applied direct to plants, for urine in a very short time becomes essentially a solution of ammonic carbonate.

Action on Human Beings and Animal Life.—The violence of the action of caustic solutions of ammonia almost entirely depends on the state of concentration.

The local action of the strong solution appears to be mainly the extraction of water and the saponifying of fat, making a soluble soap. On delicate tissues it has, therefore, a destructive action ; but S. Samuel* has shown that ammonia, when applied to the unbroken epidermis, does not have the same intense action as potash or soda, nor does it coagulate albumen. Blood, whether exposed to ammonia gas, or mixed with solution of ammonia, becomes immediately dark-red ; then, later, through destruction of the blood corpuscles, very dark, even black ; lastly, a dirty brown-red. The oxygen is expelled, the haemoglobin destroyed, and the blood corpuscles dissolved.

The albumen of the blood is changed to alkali-albuminate, and the blood itself will not coagulate. A more or less fluid condition of the blood has always been noticed in the bodies of those poisoned by ammonia.

Blood exposed to ammonia, when viewed by the spectroscope, shows the spectra of alkaline haematin, a weak absorption-band, in the neighborhood of D ; but if the blood has been acted on for some time by am-

* *Virchow's Archiv f. Path. Anat.* Bd. 51, Hft. 1 u. 2, S. 41., &c., 1870.

monia, then all absorption-bands vanish. These spectra, however, are not peculiar to ammonia, the action of caustic potash or soda being similar. The muscles are excited by ammonia, the function of the nerves are destroyed.

When a solution of strong ammonia is swallowed, there are two main effects—(1) the action of the ammonia itself on the tissues it comes into contact with, and (2) the effects of the vapour on the air-passages. There are, therefore, immediate irritation, redness, and swelling of the tongue and pharynx, a burning pain reaching from the mouth to the stomach, with vomiting, and it may be, nervous symptoms. The saliva is notably increased. In a case reported by Fonssagrives,* no less than three litres were expelled in the twenty-four hours. Often the glands under the jaw and the lymphatics of the neck are swollen.

Doses of from 5 to 30 grammes of the strong solution of ammonia may kill as quickly as prussic acid. In a case recorded by Christison,† death occurred in four minutes from a large dose, doubtless partly by suffocation. As sudden a result is also recorded by Plenk; a man, bitten by a rabid dog, took a mouthful of spirits of ammonia, and died in four minutes.

If death does not occur rapidly, there may be other symptoms—dependent not upon its merely local action, but upon its more remote effects. These mainly consist in an excitation of the brain and spinal cord, and, later, convulsive movements deepening into loss of consciousness. It has been noticed that, with great relaxation of the muscular system, the patients complain of every movement causing pain. With these general symptoms added to the local injury, death may follow many days after the swallowing of the fatal dose.

Death may also occur simply from the local injury done to the throat and larynx, and the patient may linger some time. Thus, in a case quoted by Taylor,‡ in which none of the poison appears actually to have been swallowed, the man died nineteen days after taking the poison from inflammation of the throat and larynx. As with the strong acids so with ammonia and the alkalies generally, death may also be caused many weeks and even months afterwards, from the effects of contraction of the gullet, or from the impaired nutrition consequent upon the destruction, more or less, of portions of the stomach or intestinal canal.

Post-mortem Appearances.—In recent cases there is an intense redness of the intestinal canal, from the mouth to the stomach, and even beyond, with here and there destruction of the mucous membrane, and

* *L'Union Médicale*, 1857, No. 13, p. 49, No. 22, p. 90.

† Christison, 167.

‡ "Principles of Jurisprudence," i., p. 235.

even perforation. A wax preparation in the museum of University College (No. 2,378) shows the effects on the stomach produced by swallowing strong ammonia ; it is ashen-grey in colour, and most of the mucous membrane is, as it were, dissolved away ; the cardiac end is much congested.

The contents of the stomach are usually coloured with blood ; the bronchial tubes and glottis are almost constantly found inflamed,—even a croup-like (or diphtheritic) condition has been seen. œdema of the glottis should also be looked for : in one case this alone seems to have accounted for death. The blood is of a clear-red colour, and fluid. A smell of ammonia may be present.

If a sufficient time has elapsed for secondary effects to take place, then there may be other appearances. Thus, in the case of a girl who, falling into a fainting fit, was treated with a draught of undiluted spirits of ammonia, and lived four weeks afterwards ; the stomach (preserved in St. George's Hospital museum, 43 b, ser. ix.) is seen to be much dilated and covered with cicatrices, and the pylorus is so contracted as hardly to admit a small bougie. It has also been noticed that there is generally a fatty degeneration of both the kidneys and liver.

It need scarcely be observed that, in such cases, no free ammonia will be found, and the question of the cause of death must necessarily be wholly medical and pathological.

Separation of Ammonia—Ammonia is separated in all cases by distillation, and if the organic or other liquid is already alkaline, it is at once placed in a retort and distilled. If neutral or acid, a little burnt magnesia may be added until the reaction is alkaline. It is generally laid down that the contents of the stomach in a putrid condition cannot be examined for ammonia, because ammonia is already present as a product of decomposition ; but even under these circumstances it is possible to give an opinion whether ammonia *in excess* is present. For if, after carefully mixing the whole contents of the stomach, and then drying a portion and reckoning from that weight the total nitrogen (considering for this purpose, the contents to consist wholly of albumen, which yields about 16 per cent. of nitrogen)—under these conditions, the contents of the stomach yield more than 16 per cent. of nitrogen as ammonia reckoned on the dry substance, it is tolerably certain that ammonia *not* derived from the food or the tissues is present.

If, also, there is a sufficient evolution of ammonia to cause white fumes, when a rod moistened with hydrochloric acid is brought near to the liquid, this is an effect never noticed with a normal decomposition, and renders the presence of extrinsic ammonia probable.

An alkaline-reacting distillate, which gives a brown colour with the “nessler” reagent, and which, when carefully neutralised with sul-

phuric acid, on evaporation to dryness by the careful heat of a water-bath, leaves a crystalline mass that gives a copious precipitate with platinic chloride, but is hardly at all soluble in absolute alcohol, can be no other substance than ammonia.

Estimation.—Ammonia is most quickly estimated by distilling, receiving the distillate in decinormal acid, and then titrating back. It may also be estimated as the double chloride of ammonium and platinum $(\text{NH}_4\text{Cl})_2\text{PtCl}_4$. The distillate is exactly neutralised by HCl, evaporated to near dryness, and an alcoholic solution of platinic chloride added in sufficient quantity to be always in slight excess, as shown by the yellow colour of the supernatant fluid. The precipitate is collected, washed with a little alcohol, dried, and weighed on a tared filter; 100 parts of the salt are equal to 8·6 of NH_3 .

V.—CAUSTIC POTASH AND SODA.

There is so little difference in the effects produced by potash and soda respectively, that it will be convenient to treat them together.

Potash (potassa caustica).—Hydrate of potassium (KHO), atomic weight 56, specific gravity, 2·1.

Properties.—Pure hydrate of potassium is a compact, white solid, usually met with in the form of sticks. When heated to a temperature a little under redness, it melts to a nearly colourless liquid; in this state it is intensely corrosive. It rapidly absorbs moisture from the air, and moist potash also absorbs with great avidity carbon dioxide; it is powerfully alkaline, changing red litmus to blue. It is soluble in half its weight of cold water, great heat being evolved during solution; it forms two definite hydrates—one, $\text{KHO} + \text{H}_2\text{O}$; the other, $\text{KHO} + 2\text{H}_2\text{O}$. It is sparingly soluble in ether, but is dissolved by alcohol, wood-spirit, fusel oil, and glycerine.

Pharmaceutical Preparations.—Potassium hydrate is officinal in all pharmacopœias, as well as the solution of potash. The *liquor potassæ*, or solution of potash, of the British Pharmacopœia, is a strongly alkaline, caustic liquid, of 1·058 specific gravity, and containing 15·34 per cent. by weight of KHO. It should, theoretically, not effervesce, when treated with an acid, but its affinity for CO_2 is so great that all solutions of potash, which have been in any way exposed to air, contain a little carbonate. Caustic sticks of potash and lime used to be officinal in the British Pharmacopœia. Filho's caustic is still in commerce, and is made by melting together two parts of potassium hydrate and one part of lime

in an iron ladle or vessel ; the melted mass is now moulded by pouring it into leaden moulds.

Carbonate of Potash ($K_2CO_3 + 2H_2O$), when pure, is in the form of small white crystalline grains, alkaline in taste and reaction, and rapidly deliquescent when exposed to moist air ; it gives all the chemical reactions of potassium oxide, and carbon dioxide. Carbonate of potash, under the name of *salt of tartar*, or potashes, is sold by oilmen for cleansing purposes. They supply it either in a fairly pure state, or as a darkish moist mass containing many impurities.

Bicarbonate of Potash ($KHCO_3$) is in the form of large, transparent rhombic prisms, and is not deliquescent. The effervescing solution of potash (*liquor potassæ effervescens*) consists of thirty grains of $KHCO_3$ in a pint of water (1.42 grm. per litre), and as much CO_2 as the water will take up under a pressure of seven atmospheres.

Caustic Soda.—*Sodium Hydrate* ($NaHO$).—This substance is a white solid, very similar in appearance to potassium hydrate ; it absorbs moisture from the air, and afterwards carbon dioxide, becoming solid again, for the carbonate is not deliquescent. In this respect, then, there is a great difference between potash and soda, for the former is deliquescent both as hydrate and carbonate ; a stick of potash in a semi-liquid state, by exposure to the air, continues liquid, although saturated with carbon dioxide. Pure sodium hydrate has a specific gravity of 2.0 ; it dissolves in water with evolution of heat, and the solution gives all the reactions of sodium hydrate, and absorbs carbon dioxide as readily as the corresponding solution of potash. The *liquor sodaæ* of the B. P. should contain 4.1 per cent. of $NaHO$.

Sodaæ Carbonas (*carbonate of soda*), ($Na_2CO_3 \cdot 10H_2O$).—The pure carbonate of soda for medicinal use is in colourless and transparent rhombic octahedrons ; when exposed to air, the crystals effloresce and crumble. The *sodaæ carbonas exsiccata*, or dried carbonate of soda, is simply the ordinary carbonate, deprived of its water of crystallisation, which amounts to 62.93 per cent.

Bicarbonate of Soda ($NaHCO_3$) occurs in the form of minute crystals, or, more commonly, as a white powder. The *liquor sodaæ effervescens* of the B. P. is a solution of the bicarbonate, 30 grains of the salt in 25 ounces of water (3.42 grms. per litre), the water being charged with as much carbonate acid as it will hold under a pressure of seven atmospheres. The *bicarbonate of Soda lozenges* (*trochisci sodaæ bicarbonatis*) contain in each lozenge five grains (342 grm.) of the bicarbonate. The carbonate of soda sold for household purposes is of two kinds—the one, “seconds,” of a dirty-white colour and somewhat impure ; the other, “best,” is a white mass of much greater purity. *Javelle water* (*Eau de Javelle*) is a solution of hypochlorite of soda ; its action is poi-

sonous, more from the caustic alkali than from the chlorine, and may, therefore, be here included.

Statistics.—Poisoning by the fixed alkalies is not so frequent as poisoning by ammonia. Falck has collected, from medical literature, twenty-seven cases, two of which were the criminal administering of *Eau de Javelle*, and five were suicidal ; 22, or 81.5 per cent. died—in one of the cases after twenty-four hours ; in the others, life was prolonged for days, weeks, or months—in one case for twenty-seven months.

Effects on Animal and Vegetable Life.—The fixed alkalies destroy all vegetable life, if applied in strong solution or in substance, by dehydrating and dissolving the tissues. The effects on animal tissues are, in part, due also to the affinity of the alkalies for water. They extract water from the tissues with which they come in contact, and also attack the albuminous constituents, forming alkali-albuminate, which swells on the addition of water, and, in a large quantity, even dissolves. Cartilaginous and horny tissues are also acted upon, and strong alkalies will dissolve hair, silk, &c. The action of the alkali is by no means restricted to the part first touched, but has a remarkable faculty of spreading in all directions.

Local Effects.—The effects of strong alkali applied to the epidermis are similar to, but not identical with, those produced by strong acids. S. Samuel* has studied this experimentally on the ear of the rabbit ; a drop of a strong solution of caustic alkali, placed on the ear of a white rabbit, caused stasis in the arteries and veins, with first a greenish, then a black colour of the blood ; the epidermis was bleached, the hair loosened, and there quickly followed a greenish coloration on the back of the ear, opposite to the place of application. Around the burnt spot appeared a circle of anastomosing vessels, a blister rose, and a slough separated in a few days. The whole thickness of the ear was coloured yellowish-green, and, later, the spot became of a rusty-brown.

Symptoms.—The symptoms observed when a person has swallowed a dangerous dose of caustic (fixed) alkali are very similar to those noticed with ammonia, with the important exception that there is no respiratory trouble, unless the liquid has come into contact with the glottis ; nor has there been hitherto remarked the rapid death which has taken place in a few ammonia poisonings, the shortest time hitherto recorded being three hours as related by Taylor, in a case in which a boy had swallowed three ounces of a strong solution of carbonate of potash.

There is instant pain, extending from the mouth to the stomach, a persistent and unpleasant taste ; if the individual is not a determined suicide, and the poison (as is mostly the case) has been taken accidentally,

* *Virchow's Archiv. f. Path. Anat.* Bd. 51, Hft. 1 u. 2, 1870.

the liquid is immediately ejected as much as possible, and water, or other liquid at hand, drunk freely. Shock may at once occur, and the patient die from collapse; but this, even with frightful destruction of tissue, appears to be rare. Vomiting supervenes; what is ejected is strongly alkaline, and streaked with blood, and has a soapy, frothy appearance. There may be diarrhoea, great tenderness of the abdomen, and quick pulse and fever. With caustic potash, there may be also noticed its toxic effects (apart from local action) on the heart; the pulse, in that case, is slow and weak, and loss of consciousness and convulsions are not uncommon. If the collapse and after-inflammation are recovered from, then, as in the case of the mineral acids, there is all the horrid sequence of symptoms pointing to contractions and strictures of the gullet or pylorus, and the subsequent dyspepsia, difficulty of swallowing, and not unfrequently actual starvation.

Post-mortem Appearances.—In cases of recent poisoning, spots on the cheeks, lips, clothing, &c., giving evidence of the contact of the alkali, should be looked for; but this evidence, in the case of persons who have lived a few days, may be wanting. The mucous membrane of the mouth, throat, gullet, and stomach is generally more or less white—here and there denuded, and will be found in various stages of inflammation and erosion, according to the amount taken, and the concentration of the alkali. Where there is erosion, the base of the eroded parts is not brown-yellow, but, as a rule, pale-red. The gullet is most affected at its lower part, and it is this part which is mostly subject to stricture. Thus Böhm* found that in eighteen cases of contraction of the gullet collected by him, ten of the eighteen showed the contraction at the lower third.

The changes which the stomach may present if the patient has lived some time, are well illustrated by a preparation in St. George's museum (43 a. 264, ser. ix.). It is the stomach of a woman, aged 44, who had swallowed a concentrated solution of carbonate of potash. She vomited immediately after taking it, and lived about two months, during the latter part of which she had to be nourished by injections. She died mainly from starvation. The gullet in its lower part is seen to be much contracted, its lining membrane destroyed, and the muscular coats exposed. The coats of the stomach are thickened, but what chiefly arrests the attention is a dense cicatrix at the pylorus, with an aperture so small as only to admit a probe.

The colour of the stomach is generally bright-red, but in that of a child, preserved in Guy's Hospital museum (No. 1798²¹), the mucous membrane is obliterated, the rugæ destroyed, and a dark-brown stain

* *Central Blatt für die Med. Wiss.*, 1874.

a noticeable feature. The stomach is not, however, necessarily affected. In a preparation in the same museum (No. 1798²⁰) the mucous membrane of the stomach of a child who swallowed soap-lees, is seen to be almost healthy, but the gullet is much discoloured.

The action on the blood is to change it into a gelatinous mass ; the blood corpuscles are destroyed, and the whole colour becomes of a dirty blackish-red ; the spectroscopic appearances are identical with those already described (see p. 88). The question as to the effects of chronic poisoning by the alkalies or their carbonates may arise. Little or nothing is, however, known of the action of considerable quantities of alkalies taken daily. In a case related by Dr. Tunstall,* a man for eighteen years had taken daily two ounces of bicarbonate of soda for the purpose of relieving indigestion. He died suddenly, and the stomach was found extensively diseased ; but since the man, before taking the alkali, had complained of pain, &c., it is hardly well, from this one case, to draw any conclusion.

Chemical Analysis.—The tests for potassium or sodium are too well known to need more than enumeration. The intense yellow flame produced when a sodium salt is submitted to a Bunsen flame, and the bright sodium-line at D when viewed by the spectroscope, is a delicate test ; while potassium gives a dull-red band in the red, and a faint but very distinct line in the violet. Potassium salts are precipitated by tartaric acid, while sodium salts do not yield this precipitate ; potassium salts also give a precipitate with platinic chloride insoluble in strong alcohol, while the compound salt with sodium is rapidly dissolved by alcohol or water. This fact is utilised in the separation and estimation of the two alkalies.

Estimation of the Fixed Alkalies.—To detect a fixed alkali in the contents of the stomach, a convenient process is to proceed by dialysis, and after twenty-four hours, to concentrate the outer liquid by boiling, and then, if it is not too much coloured, to titrate directly with a deci-normal sulphuric acid. After exact neutralisation, the liquid is evaporated to dryness, carbonised, the alkaline salts lixiviated out with water, the sulphuric acid exactly precipitated by baric chloride, and then, after separation of the sulphate, the liquid treated with milk of lime. On filtration, the filtrate will contain alkalies only, and to make sure that this is so, a little carbonate of ammonia is added to see whether any precipitate is produced. The liquid may now be evaporated to dryness with either hydrochloric or sulphuric acids, and the total alkalies weighed as sulphates or chlorides. Should it be desirable to know exactly the proportion of potassium to sodium, it is best to convert the alkalies into chlorides—dry gently, ignite, and weigh ; then dissolve in the

* *Med. Times*, Nov. 30, 1850, p. 564.

least possible quantity of water, and precipitate by platinic chloride, which should be added so as to be a little in excess, but not much. The liquid thus treated is evaporated nearly to dryness, and then extracted with alcohol of 80 per cent., which dissolves out any of the double chloride of platinum and sodium. Finally, the precipitate is collected on a tared filter and weighed, after drying at 100°. In this way the analyst both distinguishes between the salts of sodium and potassium, and estimates the relative quantities of each. It is hardly necessary to observe that, if the double chloride is wholly soluble in water or alcohol, sodium alone is present. This, however, will never occur in operating on organic tissues and fluids, for both alkalies are invariably present. A correction must be made when complex organic fluids are in this way treated for alkalies which may be naturally in the fluid. Here the analyst will be guided by his preliminary titration, which gives the total free alkalinity. In cases where the alkali has been neutralised by acids, of course no free alkali will be found, but the corresponding salt.

VI.—NEUTRAL SODIUM, POTASSIUM, AND AMMONIUM SALTS.

The neutral salts of the alkalies are poisonous, if administered in sufficient doses, and the poisonous effect of the sulphate, chloride, bromide, iodide, tartrate, and citrate appears to depend on the specific action of the alkali metal, rather than on the acid, or halogen in combination. According to the recent researches of Dr. Ringer and Dr. Harrington Sainsbury,* with regard to the relative toxicity of the three, as shown by their effect on the heart of a frog—first, the potassium salts were found to exert the most poisonous action, next come the ammonium, and, lastly, the sodium salts. The highest estimate would be that sodium salts are only one-tenth as poisonous as those of ammonium or potassium ; the lowest, that the sodium salts are one-fifth : although the experiments mainly throw light upon the action of the alkalies on one organ only, yet the indications obtained probably hold good for the organism as a whole, and are pretty well borne out by clinical experience.

Sodium Salts.—Common salt in such enormous quantity as half a pound to a pound has destroyed human life, but these cases are so exceptional, that the poisonous action of sodium salts is of scientific rather than practical interest.

Potassium Salts.—Leaving for future consideration the nitrate and

* *Lancet*, June 24, 1882.

the chlorate of potassium, potassic sulphate and tartrate are substances which have destroyed human life.

Potassic Sulphate (K_2SO_4) is in the form of colourless rhombic crystals, of bitter saline taste. It is soluble in 10 parts of water.

Hydropotassic Tartrate ($KHC_4H_4O_6$), when pure, is in the form of rhombic crystals, tasting feebly acid. It is soluble in 210 parts of water at 17° .

Statistics.—There appear to be four cases on record of poisoning by the neutral salts; none of them belong to recent times, but lie between the years 1837–1856. Hence, the main knowledge which we possess of the poisonous action of the potassium salts is derived from experiments on animals.

Action on the Frog's Heart.—Both excitability and contractility are affected to a powerful degree. There is a remarkable slowing of the pulsations, irregularity, and, lastly, cessation of pulsation altogether.

Action on Warm Blooded Animals.—If a toxic solution of a potassic salt is injected into the blood-vessels of an animal, there is almost immediate death from arrest of the heart's action. Smaller doses, subcutaneously applied, produce slowing of the pulse, dyspnoea, and convulsions, ending in death. Small doses produce a transitory diminution of the force of arterial pressure, which quickly passes, and the blood-pressure rises. There is at first, for a few seconds, increase in the number of pulsations, but later a remarkable slowing of the pulse. The rise in the blood-pressure occurs even after section of the spinal cord, somewhat larger doses cause rapid lowering of the blood-pressure, and apparent cessation of the heart's action; but if the thorax be then open, the heart is seen to be contracting regularly, making some 120–160 rhythmic movements in the minute. If the respiration be now artificially maintained, and suitable pressure made on the walls of the chest, so as to empty the heart of blood, the blood-pressure quickly rises, and natural respiration may follow. An animal which lay 36 minutes apparently dead was in this way brought to life again (Böhm). The action of the salts of potassium on the blood is the same as that of sodium salts. The blood is coloured a brighter red, and the form of the corpuscles changed; they become shrivelled through loss of water. Voluntary muscle loses quickly its contractility when a solution of potash is injected into its vessels. Nerves also, when treated with a 1 per cent. solution of potassic chloride, become inexcitable.

Elimination.—The potassium salts appear to leave the body through the kidneys, but are excreted much more slowly than the corresponding sodium salts. Thus, after injection of 4 grms. of potassic chloride—in the first sixteen hours 748 grm. of KCl were excreted in the urine, and in the following twenty-four hours 2.677 grms.

Nitrate of Potash (KNO₃).—Pure potassic nitrate crystallises in large anhydrous hexagonal prisms with dihedral summits; it does not absorb water, and does not deliquesce. Its fusing point is about 340°; when melted it forms a transparent liquid, and loses a little of its oxygen, but this is for the most part retained by the liquid to be given off when the salt solidifies. At a red-heat it evolves oxygen, and is reduced first to nitrite; if the heat is continued, potassic oxide remains. The specific gravity of the fused salt is 2.06. It is not very soluble in cold water, 100 parts dissolving only 26 at 15.6°; but boiling water dissolves it freely, 100 parts dissolving 240 of the salt.

A solution of nitrate of potash, when treated with a zinc couple (see vol. i., "Foods," p. 519), is decomposed, the nitrate being first reduced to nitrite, as shown by its striking a red colour with metaphenylenediamine, and then the nitrate farther decomposing, and ammonia appearing in the liquid. If the solution is alkalised, and treated with aluminium foil, hydrogen is evolved, and the same effect produced. As with all nitrates, potassic nitrate, on being heated in a test tube with a little water, some copper filings, and sulphuric acid, evolves red fumes of nitric peroxide.

Statistics.—Potassic nitrate, under the popular name of "nitre," is a very common domestic remedy, and is also largely used as a medicine for cattle. There appear to be twenty cases of potassic nitrate poisoning on record—of these, eight were caused by the salts having been accidentally mistaken for magnesic sulphate, sodic sulphate, or other purgative salt; two cases were due to a similar mistake for common salt. In one instance, the nitrate was used in strong solution as an enema, but most of the cases were due to the taking of too large an internal dose.

Uses in the Arts, &c.—Both sodic and potassic nitrates are called "nitre" by the public indiscriminately. Sodic nitrate is imported in large quantities from the rainless districts of Peru as a manure. Potassic nitrate is much used in the manufacture of gunpowder, in the preservation of animal substances, in the manufacture of gun cotton, of sulphuric and nitric acids, &c. The maximum medicinal dose of potassium nitrate is usually stated to be 30 grains (1.9 grms.).

Action of Nitrates of Sodium and Potassium.—Both of these salts are poisonous. Potassic nitrate has been taken with fatal result by man; the poisonous nature of sodic nitrate is established by experiments on animals. The action of the nitrates of the alkalies is separated from that of the other neutral salts of potassium, &c., because in this case the toxic action of the combined nitric acid plays no insignificant part. Large doses, 3-5 grms. (46.3-77.2 grains) of potassic nitrate cause considerable uneasiness in the stomach and bowels; the digestion is disturbed; there may be vomiting and diarrhoea, and there is

generally present a desire to urinate frequently. Still larger doses, 15·30 grms. (231·5-463 grains), rapidly produce all the symptoms of acute gastro-enteritis—great pain, frequent vomiting (the ejected matters being often bloody), with irregularity and slowing of the pulse ; weakness, cold sweats, painful cramps in single muscles (especially in the calves of the legs) ; and, later, convulsions, aphonia, quick collapse, and death.

In the case of a pregnant woman, a handful of "nitre" taken in mistake for Glauber's salts produced abortion after half-an-hour. The woman recovered. Sodic nitrate subcutaneously applied to frogs kills them, in doses of '026 grm. ('4 grain), in about two hours ; there are fibrillar twitchings of single groups of muscles and narcosis. The heart dies last, but after ceasing to beat may, by a stimulus, be made again to contract. Rabbits, poisoned similarly by sodic nitrate, exhibit also narcotic symptoms ; they lose consciousness, lie upon their side, and respond only to the sharpest stimuli. The breathing, as well as the heart, is "slowed," and death follows after a few spasmoid inspirations.

Sodic nitrite was found by Barth to be a more powerful poison, less than 6 mgrms. ('1 grain) being sufficient to kill a rabbit of 455·5 grms. (7·028 grains) weight when subcutaneously injected. The symptoms were very similar to those produced by the nitrate.

The *post-mortem* appearances from potassic nitrate are as follows :—An inflamed condition of the stomach, with the mucous membrane dark in colour, and readily tearing ; the contents of the stomach are often mixed with blood. In a case related by Orfila, there was even a small perforation by a large dose of potassic nitrate, and a remarkable preservation of the body was noted.

It is believed that the action of the nitrates is to be partly explained by a reduction to nitrites, circulating in the blood as such. To detect nitrites in the blood, the best method is to place the blood in a dialyser, the outer liquid being alcohol. The alcoholic solution may be evaporated to dryness, extracted with water, and then tested by metaphenylene-diamine.

Potassic Chlorate ($KClO_3$).—Potassic chlorate is in the form of colourless, tabular crystals with four or six sides. About 6 parts of the salt are dissolved by 100 of water at 15° , the solubility increasing with the temperature, so that at 100° nearly 60 parts dissolve ; if strong sulphuric acid be dropped on the crystals, peroxide of chlorine is evolved ; when rubbed with sulphur in a mortar, potassic chlorate detonates. When the salt is heated strongly, it first melts and then decomposes, yielding oxygen gas, and is transformed into the perchlorate. If the heat is continued, this also is decomposed, and the final result is potassic chloride.

Uses.—Potassic chlorate is largely used as an oxidiser in calico printing, and in dyeing, especially in the preparation of aniline black. A

considerable quantity is consumed in the manufacture of lucifer matches and fireworks ; it is also a convenient source of oxygen. Detonators for exploding dynamite are mixtures of fulminate of mercury and potassic chlorate. It is employed as a medicine both as an application to inflamed mucous membranes, and for internal administration ; about 2,000 tons of the salt for these various purposes are manufactured yearly in the United Kingdom.

Poisonous Properties.—The facility with which potassic chlorate parts with its oxygen by the aid of heat, led to its very extensive employment in medicine. No drug, indeed, has been given more recklessly, or on a less scientific basis. Wherever there were sloughing wounds, low fevers, and malignant sore throats, especially those of a diphtheritic character, the practitioner administered potassic chlorate in colossal doses. If the patient died, it was ascribed to the malignity of the disease—if he recovered, to the oxygen of the salt ; and it is possible, from the light which of recent years has been thrown on the action of potassic chlorate, that its too reckless use has led to many unrecorded accidents.

Experiments on Animals.—F. Marchand * has studied the effects of potassic chlorate on animals, and on blood. If either potassic chlorate or sodic chlorate is mixed with fresh blood, it shows after a little while peculiar changes ; the clear red colour at first produced passes, within a few hours, into a dark red-brown, which gradually becomes pure brown. This change is produced by a 1 per cent. solution, in from fifteen to sixteen hours ; and a 4 per cent. solution at 15° destroys every trace of oxyhaemoglobin within four hours. Soon the blood takes a syrupy consistence, and, with a 2-4 per cent. solution of the salt, passes into a jelly-like mass. The jelly has much permanence, and resists putrefactive changes for a long time.

Marchand fed a dog of 17 kilos. in weight with 5 grms. of potassic chlorate for a week. As there were no apparent symptoms, the dose was doubled for two days ; and as there was still no visible effect, 50 grms. of sodic chlorate were given lastly in 5 doses. In the following night the dog died. The blood was found after death to be of a sepia-brown colour, and remained unaltered when exposed to the air. The organs were generally of an unnatural brown colour ; the spleen was enormously enlarged ; the kidneys were swollen, and of a dark chocolate brown—on section, almost black-brown, the colour being nearly equal, both in the substance and in the capsule. A microscopical examination of the kidney showed the canaliculi to be filled with brownish cylinders consisting of altered blood. A spectroscopic examination of the blood showed weak haemoglobin bands, and a narrow band in the red. With farther dilution, the haemoglobin bands vanished, but the band in the red remained.

* *Virchow's Archiv f. Path. Anat.* Bd. 77, Hft. 3, S. 455, 1879.

The diluted blood, when exposed to the light, still remained of a coffee-brown colour ; and on shaking, a white-brown froth was produced on the surface.

A second experiment, in which a hound of from 7-8 kilos. in weight was given 3-5 grm. doses of potassic chlorate in sixteen hours, and killed by bleeding seven to eight hours after the last dose, showed very similar appearances. The kidneys were intensely congested, and the peculiar brown colour was noticeable.

Effects on Man.—I find in literature thirty-nine cases recorded, in which poisonous symptoms were directly ascribed to the action of chlorate of potassium ; twenty-eight of these terminated fatally. A quadruple instance of poisoning, recorded by Brouardel and L'Hote,* illustrates many of the points relative to the time at which the symptoms may be expected to commence, and the general aspect of potassic chlorate poisoning. The “supérieure” of a religious institution was in the habit of giving, for charitable purposes, a potion containing 15 grms. (3·8 drms.) of potassic chlorate, dissolved in 360 cc. (about 12½ oz.) of a vegetable infusion.

This potion was administered to four children—viz, David, aged 2½ ; Cousin, 3½ ; Salmont, 2½ ; and Guérin, 2½. David took the whole in two and a half hours, the symptoms commenced after the potion was finished, and the child died five and a half hours after taking the first dose ; there were vomiting and diarrhoea. Cousin took the medicine in seven hours ; the symptoms also commenced after the last spoonful, and the death took place eight and a half hours from the first spoonful. The symptoms were mainly those of great depression ; the lips were blue, the pulse feeble, there was no vomiting, no diarrhoea. Salmont took the medicine in nine hours, and died in twelve. There was some diarrhoea, the stools were of a green colour. Guérin took the whole in two hours ; the symptoms commenced in four hours ; the lips were very pale, the gums blue. Death took place in four days.

There was an autopsy in the case of David only. The stomach showed a large ecchymosis on its mucous membrane, as if it had been burnt by an acid ; the spleen was gorged with blood, and its tissue friable ; the kidneys do not seem to have been thoroughly examined, but are said to have been tumefied. Potassic chlorate was discovered by dialysis. In the cases of the children just detailed, the symptoms appear to be a mixture of the depressing action of the potassium, and irritant action of the chlorate.

In adults, the main symptoms are those of nephritis, and the fatal dose for an adult is somewhere about an ounce (28·3 grm.), but half this

* *Annales d'Hygiène publique.* 1881, p. 232.

quantity would probably be dangerous, especially if given to a person who had congestion or disease of the kidneys.

Dr. Jacobi* gives the following cases.

Dr. Fountain in 1858, experimenting on himself, took 29.2 grms. (9 drms.) of potassic chlorate; he died on the seventh day from nephritis. A young lady swallowed 30 grms. (9.2 drms.), when using it as a gargle; she died in a few days from nephritis. A man, thirty years of age, died in four days after having taken 48 grms. (12.3 drms.) of sodic chlorate in six hours. The *shortest time* in which I can find the salt to have been fatal, is a case related by Dr. Manouvriez, in which a woman took 45 grms., and died in five hours. The *smallest dose* which has proved fatal is one in which an infant three years old was killed by 3 grms. (46.3 grains).

Jacobi considers that the maximum dose to be given in divided doses during the twenty-four hours, to infants under three, should be from 1-1.5 grm. (23.1 grains), to children from three years old, up to 2 grm. (30.8 grains); and adults from 6-8 grm. (92.6-123.4 grains).

Elimination.—Potassic chlorate is quickly absorbed from mucous membranes, and by the inflamed skin, and rapidly separated from the body by the action of the kidneys. Wöhler, as early as 1824, recognised that it in great part passed out of the body unchanged, and, lately, Isambert, in conjunction with Hirne † making quantitative estimations, recovered from the urine no less than 95 per cent. of the ingested salt. Otto Hehner has also made several auto-experiments, and taking two and a half drachms, found that it could be detected in the urine an hour and a half afterwards. At that time 17.23 per cent. of the salt had been excreted, and, by the end of eleven hours, 93.8 per cent. was recovered. It is then difficult to believe that the salt gives any oxygen to the tissues, for though it is true that in all the investigations a small percentage remains to be accounted for, and also that Binz ‡ making experiments by mixing solutions of potassic chlorate with moist organic substances, such as pus, yeast, fibrin, &c., has declared that at a blood heat, the chlorate is rapidly reduced, and is no longer recognisable as chlorate—yet, it may be affirmed, that potassic chlorate is recovered from the urine as completely as anything which is ever excreted by the body, and that deductions drawn from the changes undergone by the salt in solutions of fibrin, &c., have only an indirect bearing on the question.

The essential action of potassic chlorate seems to be that it causes a peculiar change in the blood, acting on the colouring matter and corpus-

* *Amer. Med. Times*, 1860.

† *Gaz. Méd. de Paris*, 1875. Nro. 17, 35, 41, 43.

‡ *Berlin Klin. Wochenschr.* xi. 10, S. 119, 1874.

cles ; the latter lose their property as oxygen carriers ; the haemoglobin is in part destroyed ; the corpuscles dissolved. The decomposed and altered blood-corpuscles are crowded into the kidneys, spleen, &c. : they block up the uriniferous canaliculi, and thus the organs present the curious colouring seen after death, and the kidneys become inflamed.

DETECTION AND ESTIMATION OF POTASSIC CHLORATE.

Organic fluids are best submitted to dialysis ; the dialysed fluid should then be concentrated and qualitative tests applied. One of the best tests for the presence of a chlorate is, without doubt, that recommended by Fresenius. The fluid to be tested is acidulated with a few drops of sulphuric acid ; sulphate of indigo added sufficient to colour the solution blue, and finally a few drops of sulphurous acid. In presence of potassic or sodic chlorate, the blue colour immediately vanishes. This method is capable of detecting 1 part in 128,000 ; provided the solution is not originally coloured, and but little organic matter is present.

The urine can be examined direct, but if it contain albumen, the blue colour may disappear and yet chlorate be present ; if too much sulphurous acid be also added, the test may give erroneous results. These are but trivial objections, however, for if the analyst obtains a response to the test, he will naturally confirm or disprove it by the following process :—

The liquid under examination, organic or otherwise, is divided into two equal parts. In the one, all the chlorine present is precipitated as chloride, by silver nitrate in the usual way, and the chloride of silver collected and weighed. In the other, the liquid is evaporated to dryness and well charred by a dull red heat, the ash dissolved in weak nitric acid, and the chlorides estimated as in the first case. If chlorates were present, there will be a difference between the two estimations, proportionate to the amount of chlorates which have been converted into chlorides by the carbonisation, and the first silver chloride subtracted from the second will give an argentic chloride which is to be referred to chlorate. In this way also the amount present may be quantitatively estimated, 100 parts of silver chloride equalling 85·36 of potassic chlorate.

TOXICOLOGICAL DETECTION OF ALKALI SALTS.—

(See also *ante*, p. 95.)

Sodium, in combination, especially with chlorine, and also with sulphuric, carbonic, and phosphoric acids, is found in the plasma of the blood, in the urinary secretion, in the pancreatic juice, in human bile, and in serous transudations, &c. Potassium, in combination, is especially found

in the red blood-corpuscles, in the muscles, in the nervous tissues, and in milk. Ammonia, in combination with acids, is naturally found in the stomach, in the contents of the intestines ; it is also a natural constituent of the blood in small traces, and in a corpse is copiously evolved from putrefactive changes.

It hence follows, that mere qualitative tests for these elements in the tissues or fluids of the body are of not the slightest use, for they are always present during the life of the healthiest individual, and can be found after death in persons dying from any malady whatever. To establish the fact of a person having taken an unusual dose of any of the alkali salts, by simple chemical evidence, it must be proved that the alkalies are present in unusual quantities or in an abnormal state of combination.

In cases of rapid death, caused by sodic or potassic salts, they will be found in such quantity in the contents of the stomach, or in matters vomited, that there will probably be no difficulty in coming to a direct conclusion ; but if some time has elapsed, the analyst may not find a sufficient ground for giving a decided judgment, the excretion of the alkali salts being very rapid.

In most cases, it will be well to proceed as follows :—The contents of the stomach are, if necessary, diluted with distilled water, and divided into three parts, one of which is submitted to dialysis, and then the dialysed liquid evaporated to a small bulk and examined qualitatively, in order to ascertain whether a large amount of alkaline salts is present, and in what form. In this way, the presence or absence of nitrate of potassium or sodium may be proved, or the iodide, bromide, sulphate, and chlorate detected.

To find in this way, nitrate of potassium, a coarse test is preferable to the finer tests dependent upon conversion of the nitrate into nitrites or into ammonia, for these tests are so delicate, that nitrates may be detected in traces ; whereas, in this examination, to find traces is of no value. Hence, the old-fashioned test of treating the concentrated liquid in a test-tube with copper filings and then with sulphuric acid, and looking for the red fumes, is best, and will act very well, even should, as is commonly the case, some organic matters have passed through the dialyser.

Chlorates are indicated if the liquid is divided into two parts and tested in the manner recommended on page 103. If present in any quantity, chlorates or nitrates may be indicated by the brilliant combustion of the organic matter when heated to redness, as also by the action of strong sulphuric acid on the solid substances—in the one case, yellow vapours of peroxide of chlorine being evolved—in the other, the red fumes already mentioned of nitric peroxide.

With regard to a substance such as the hydro-potassic tartrate, its insolubility in water renders it not easy of detection by dialysis; but its very insolubility will aid the analyst, for the contents of the stomach may be treated with water, and thus all soluble salts of the alkalies extracted. On now microscopically examining the insoluble residue, crystals of bitartrate, if present, will be readily seen. They may be picked up on a clean platinum wire and heated to redness in a Bunsen flame, and spectroscopically examined. After heating, the melted mass will have an alkaline reaction, and give a precipitate with platinic chloride. All other organic salts of potassium are soluble, and a white crystal giving such reaction must be hydro-potassic tartrate.

Ammonium Salts.—If the body is fresh, and yet the salts of ammonium present in large amount, it is safe to conclude that they have an external origin; but there might be some considerable difficulty in criminal poisoning by a neutral salt of ammonium, and search for it in a highly putrid corpse. Probably, in such an exceptional case, there would be other evidence. With regard to the quantitative separation and estimation of the fixed alkalies in the ash of organic substances, the reader is referred to the processes given in vol. i., "Foods," p. 101, *et seq.*, and in the present work, p. 95.

PART IV.—MORE OR LESS VOLATILE POISONOUS SUBSTANCES
CAPABLE OF BEING SEPARATED BY DISTILLATION FROM
NEUTRAL OR ACID LIQUIDS.

HYDROCARBONS—CAMPHOR—
ALCOHOL—AMYL NITRITE—ETHER—CHLOROFORM—
AND OTHER ANÆSTHETICS—CHLORAL—CARBON DISUL-
PHIDE—CARBOLIC ACID—NITRO-BENZENE—PRUSSIC
ACID—PHOSPHORUS.

I.—HYDROCARBONS.

1.—PETROLEUM.

Petroleum is a general term for a mixture of hydrocarbons of the parraffin series, which are found naturally in certain parts of the world, and are in commerce under liquid and solid forms of various density. Crude petroleum is not imported into England, the original substance having previously undergone more or less rectification. The lighter and more volatile portions are known under the name of cymogene, rhigolene, gasolene, and naphtha.

Cymogene has a specific gravity of .590, and boils at 0°. It has been employed in refrigerating machines. It appears to consist chiefly of butane, (C_4H_{10}).

Rhigolene is now used in medicine in the form of spray to produce local anaesthesia. It boils at 18°, and has a density of .650.

Gasolene has a density of .680—.688; it has received technical applications in the “naphthalising” of air and gas.

Benzoline (*mineral naphtha*, *petroleum naphtha*, *petroleum spirit*, *petroleum ether*) is a mixture of the lighter series of hydrocarbons; the greater part consists of heptane, and there is also a considerable quantity of pentane (C_5H_{12}) present. The specific gravity varies from .69 to .74. It is very inflammable, and is used in sponge lamps, and also as a solvent for gutta-percha, naphthalene, parraffin, wax, and many other bodies. By the practical chemist it is much employed.

The similarity of the terms *benzoline* and *benzene* has caused benzoline to be often confused with *benzol* or *benzene*, the leading constituent of coal-tar naphtha, C_6H_6 . Mr. Allen* gives in the following table a summary of the chief points of distinction, both between petroleum, naphtha, shale naphtha, and coal-tar naphtha. The table is founded upon the examination of particular samples, and commercial samples may present a few minor deviations.

TABLE VI.—VARIETIES OF NAPHTHA.

Petroleum Naphtha.	Shale Naphtha.	Coal-tar Naphtha.
Contains at least 75 per cent. of heptane, C_7H_{16} , and other hydrocarbons of the marsh gas or paraffin series; the remainder apparently olefins C_nH_{2n} , with distinct traces of benzene and its homologues.	Contains at least 60 to 70 per cent. of heptylene, C_7H_{14} , and other hydrocarbons of the olefin series; the remainder paraffins. No trace of benzene or its homologues.	Consists almost wholly of benzene, C_6H_6 , and other homologous hydrocarbons, with a small per centage of light hydrocarbons in some samples.
Specific gravity at 15°, .600.	Specific gravity at 15°, .718.	Specific gravity .876.
Distils between 65° and 100°.	Distils between 65° and 100°.	Distils between 80° and 120°.
Dissolves coal-tar pitch, but slightly; liquid, but little coloured even after prolonged contact.	Behaves similarly to petroleum naphtha with regard to the solution of pitch.	Readily dissolves pitch, forming a deep brown solution.
On shaking three measures of the sample with one measure of fused crystals of absolute carbolic acid, no solution. Liquids not miscible.	When treated with fused carbolic acid crystals, the liquids mix perfectly.	The liquids form a homogeneous mixture when treated with fused carbolic acid crystals.
Combines with 10 per cent. of its weight of bromine in the cold.	Combines with upwards of 90 per cent. of its weight of bromine.	Combines slowly with 30-40 per cent. of its weight of bromine.

Paraffin oil (or *kerosine*, *mineral oil*, *photogen*, &c.) is the chief product resulting from the distillation of American petroleum—the usual specific gravity is about .802—it is a mixture of hydrocarbons of the paraffin series. It should be free from the more volatile constituents, and hence should not take fire when a flame is applied near the surface of the cold liquid.

Effects of Petroleum.—Since we have here to deal with a commercial

* "Commercial Organic Analysis," vol. ii., 31.

substance of such different degrees of purity, and various samples of which are composed of such various proportions of different hydrocarbons, its action can only be stated in very general terms. Eulenberg* has experimented with the lighter products obtained from the distillation of Canadian petroleum. This contained sulphur products, and was extremely poisonous, the vapour killing a rabbit in a short time, with previous insensibility and convulsions. The autopsy showed a thin extravasation of blood on the surface of each of the bulbi, much coagulated blood in the heart, congested lungs, and a bloody mucous covering the tracheal mucous membrane. An experiment made on a cat with the lighter petroleum (which had no excess of sulphur) in the state of vapour, showed that it was an anaesthetic, the anaesthesia being accompanied by convulsions, which towards the end were tetanic and violent. The evaporation of 1.5 grm. in a close chamber killed the animal in three hours. The lungs were found congested, but little else was remarkable. Much petroleum-vapour is breathed in certain factories, especially those in which petroleum is refined.† From this cause there have been rather frequent toxic symptoms among the workmen. Eulenberg‡ describes the symptoms as follows:—A person, after breathing an overdose of the vapour, becomes very pale, the lips are livid, the respiration slow, the heart's action weak and scarcely to be felt. If he does not immediately go into the open air away from the poisonous vapour, these symptoms may pass on to insensibility, convulsions, and death. It often occasions a condition of the voluntary muscles similar to that induced by drunkenness, and on recovery the patient is troubled by singing in the ears and noises in the head. The smell and taste of the poison may remain for a long time.

Poisoning by taking light petroleum into the stomach is not common. In a case recorded by Taylor,§ a woman, for the purpose of suicide, swallowed a pint of petroleum. There followed a slight pain in the stomach, and a little febrile disturbance, and a powerful smell of petroleum remained about the body for six days; but she completely recovered. In August, 1870, a sea-captain drank a quantity of paraffin, that is, lighting petroleum, and died in a few hours in an unconscious state. A child, two years old, was brought to King's College Hospital within ten minutes after taking a teaspoonful of paraffin. It was semi-comatose and pale, with contracted pupils; there was no vomiting or

* *Gewerbe Hygiène.*

† The vapour most likely to rise at the ordinary temperature, and mix with the atmosphere, is that of the lighter series, from cymogene to benzoline.

‡ *Op. cit.*

§ "Poisons," p. 656.

purgings. Emetics of sulphate of zinc were administered, and the child recovered in twenty-four hours. In another case treated at the same hospital, a child had swallowed an unknown quantity of paraffin. It fell into a comatose state, which simulated tubercular meningitis, and lasted for nearly three weeks.* In a case recorded by Mr. Robert Smith,† a child, 4 years of age, had swallowed an unknown quantity of paraffin. A few minutes afterwards, the symptoms commenced ; they were those of suffocation, with a constant cough ; there was no expectoration ; the tongue, gums, and cheeks, were blanched and swollen where the fluid touched them ; recovery followed. A woman, aged 32, who had taken a quarter of a pint of paraffin, was found unconscious and very cold ; the stomach pump was used, and she recovered.‡ Hence it is tolerably certain, from the above instances, that should a case of petroleum poisoning occur, the expert will not have to deal with infinitesimal quantities, but while the odour of the oil will probably be distinctly perceptible, there will be also a sufficient amount obtained either from matters vomited, or the contents of the stomach, &c., so that no difficulty will be experienced in identifying it.

In order to separate petroleum from any liquid, the substances under examination must be carefully distilled in the manner recommended under "*Ether*." The lighter petroleums will distil by the aid of a water-bath ; but the heavier require a stronger heat ; redistillation of the distillate may be necessary. The odour of the liquid, its inflammable character, and its other properties, will be sufficient for identification.

2. COAL-TAR NAPHTHA—BENZENE.

Coal-tar naphtha, in its crude state, is an extremely complex liquid, of a most disagreeable smell. Much benzene, (C_6H_6), is present with higher homologues of the benzene series. Toluene, (C_7H_8), naphthalene, ($C_{10}H_8$), hydrocarbons of the paraffin series, especially hexane, (C_6H_{14}), and hydrocarbons of the olefin series, especially pentylene, hexylene, and heptylene, (C_5H_{10} , C_6H_{12} and C_7H_{14}). Besides these, there are nitrogenised bases, such as aniline, picoline, and pyridine ; phenols, especially carbolic acid ; ammonia, ammonium sulphide, carbon disulphide, and probably other sulphur compounds ; acetylene and aceto-nitrile. By distillation and fractional distillation are produced what are technically known as "once

* *Brit. Med. Journ.*, Sept. 16, 1876, p. 365.

† *Brit. Med. Journ.*, Oct. 14, 1876.

‡ *Pharm. Journ.*, Feb. 12, 1875 ; also four other cases see *Brit. Med. Journal*, Nov. 4, 1876 ; and Köhler's "*Physiol. Therap.*," p. 487.

"run" naphtha, 90 per cent. benzol, 50 and 90 per cent. benzol,* 30 per cent. benzol, solvent naphtha, and residue known as "last runnings."

Taylor† records a case in which a boy aged 12 swallowed about three ounces of naphtha, the kind usually sold for burning in lamps, and died with symptoms of narcotic poisoning. The child, after taking it, ran about in wild delirium, he then sank into a state of collapse, breathing stertorously, and the skin became cold and clammy. On vomiting being excited, he rejected about two tablespoonfuls of the naphtha, and recovered somewhat, but again fell into collapse with great muscular relaxation. The breathing was difficult; there were no convulsions; the eyes were fixed and glassy, the pupils contracted; there was frothing at the mouth. In spite of every effort to save him, he died in less than three hours after taking the poison. The body, examined three days after death, smelt strongly of naphtha, but the *post-mortem* appearances were in no way peculiar, save that the stomach contained a pint of semi-fluid matter, from which a fluid, having the characteristics of impure benzene, was separated.

The effects of the vapour of benzene have been studied by Eulenberg in experiments on cats and rabbits, and there are also available observations on men,‡ who have been accidentally exposed to its influence. From these sources of information, it is evident that the vapour of benzene has a distinctly narcotic effect, while influencing also in a marked degree the spinal cord. There are, as symptoms, noises in the head, convulsive trembling and twitchings of the muscles, with difficulty of breathing.

DETECTION AND SEPARATION OF BENZENE.

Benzene is separated from liquids by distillation, and may be recognised by its odour, and by the properties described at page 107. The best process of identification, perhaps, is to purify and convert it into nitro-benzene, and then into aniline, in the following manner:—

Purification.—The liquid is agitated with a solution of caustic soda; this dissolves out of the benzene any bodies of an acid character, such as phenol, &c. The purified liquid should again be distilled, collecting that portion of the distillate which passes over between 65° and 100°; directly the thermometer attains nearly the 100°, the distillation should be

* Or 50/90 benzol, this indicates that 50 per cent. distils over below 100; and 40, making in all 90, below 120°.

† *Op. cit.*, p. 657.

‡ Dr. Stone, *Med. Gaz.*, 1848. Vol. xii., p. 1077.

stopped. The distillate, which contains all the benzene present, is next shaken with concentrated sulphuric acid in the cold ; this will dissolve out all the hydrocarbons of the ethylene and acetylene series. On removing the layer of benzene from the acid, it must be again shaken up with dilute soda, so as to remove every trace of acid. The benzene is, by this rather complicated series of operations, obtained in a very fair state of purity, and may be converted into nitro-benzene, as follows :—

Conversion into Nitro-Benzene.—The oily liquid is placed in a flask, and treated with four times its volume of fuming nitric acid. The flask must be furnished with an upright condenser ; a vigorous action mostly takes place without the application of heat, but if this does not occur, the flask may be warmed for a few minutes.

After the conversion is over, the liquid, while still warm, must be transferred into a burette furnished with a glass tap, or to a separating funnel, and all except the top layer, run into cold water ; if benzene was originally present, either oily drops of nitro-benzene will fall, or if the benzene was only in small quantity, a fine precipitate will gradually settle down to the bottom of the vessel, and a distinct bitter-almond smell be observed ; but, if there was no benzene in the original liquid, and, consequently, no nitro-benzene formed, no such appearance will be observed.

Conversion into Aniline.—The nitro-benzene may itself be identified by collecting it on a wet filter, dissolving it off the filter by alcohol, acidifying the alcoholic solution by hydrochloric acid, and then boiling it for some time with metallic zinc. In this way aniline is formed by reduction. On neutralising and diluting the liquid, and cautiously adding a little clear solution of bleaching powder, a blue or purple colour passing to brown is in a little time produced.

3. TERPENES—ESSENTIAL OILS—OIL OF TURPENTINE.

The terpenes are hydrocarbons of the general formula C_nH_{2n-4} . The natural terpenes are divided into three classes :—

1. *The true terpenes, formula* ($C_{10}H_{16}$)*, a large number of essential oils, such as those of turpentine, orange peel, nutmeg, caraway, anise, thyme, &c., are mainly composed of terpenes.*

2. *The cedrenes formula* ($C_{15}H_{24}$)—the essential oil of cloves, rose-wood, cubeb, calamus, cascarilla, and patchouli, belong to this class.

3. *The colophene hydrocarbons, formula* ($C_{20}H_{32}$)*, represented by colophony.*

Of all these, oil of turpentine alone has any toxicological significance ; it is, however, true that all the essential oils, if taken in considerable doses, are poisonous, and cause, for the most part, vascular excite-

ment and complex nervous phenomena, but their action has not been very completely studied. They may all be separated by distillation, but a more convenient process for recovering an essential oil from a liquid is to shake it up with petroleum ether, separating the petroleum and evaporating spontaneously; by this means the oil is left in a fair state of purity.

4. OIL OF TURPENTINE—SPIRITS OF TURPENTINE— “TURPS”—CAMPHENENE.

Various species of pine yield a crude turpentine, holding in solution more or less resin. The turpentine may be obtained from this exudation by distillation, and when the first portion of the distillate is treated with alkali, and then redistilled, the final product is known under the name of “rectified oil of turpentine,” and is sometimes called “camphene.” It mainly consists of terebenthene. Terebenthene obtained from French turpentine differs in some respects from that obtained from English or American turpentine. They are both mobile, colourless liquids, having the well-known odour of turpentine and highly refractive; but the French terebenthene turns a ray of polarised light to the left— 40.3° for the sodium ray, and the English to the right $+21.5^\circ$; the latter terebenthene is known scientifically as austra-terebenthene. This action on polarised light is retained in the various compounds and polymers of the two turpentine oils.

The specific gravity of turpentine oil is .864; its boiling point, when consisting of pure terebenthene 156° , but impurities may raise it up to 160° ; it is combustible and burns with a smoky flame. Oil of turpentine is very soluble in ether, petroleum ether, carbon disulphide, chloroform, benzene, fixed and essential oils, and by the use of these solvents it is conveniently separated from the contents of the stomach. It is insoluble in water, glycerine, and dilute alkaline and acid solutions; and very soluble in absolute alcohol, from which it may be precipitated by the addition of water.

It is polymerised by the action of strong sulphuric acid, the polymer of course, boiling at a higher temperature than the original oil. With water it forms a crystalline hydrate, $(C_{10}H_{20}O_2H_2O)$. On passing nitrosyl chloride gas into the oil, either pure or diluted with chloroform or alcohol, the mixture being cooled by ice, a white crystalline body is deposited, of the formula $C_{10}H_{16}(NOCl)$. By treating this compound with alcoholic potash, the substitution product, $(C_{10}H_{16}NO)$, is obtained. By treating turpentine with an equal bulk of warm water, and shaking it in a large bottle with air, camphoric acid and peroxide of hydrogen are formed. When turpentine oil is left in contact with concentrated hydro-

chloric acid, there is formed terebenthene dihydrochloride, ($C_{10}H_{16} \cdot 2HCl$), which forms rhombic plates, insoluble in water, and decomposable by boiling alcoholic potash, with formation of terpinol ($C_{10}H_{17} \cdot O$). The dihydrochloride gives a colour-reaction with ferric chloride. This is an excellent test—not, it is true, confined to oil of turpentine—but common to the dihydrochlorides of all the terpenes. A few drops of the oil are stirred in a porcelain capsule with a drop of hydrochloric acid, and one of ferric chloride solution; on gently heating, there is produced first a rose colour, then a violet-red, and lastly a blue.

Effects of the Administration of Turpentine.—L. W. Liersch * exposed animals to the vapour of turpentine, and found that a cat and a rabbit died within half-an-hour. There was observed uneasiness, reeling, want of power in the limbs (more especially in the hinder extremities), convulsions, partial or general, difficulty of respiration; and the heart's action was quickened. Death took place, in part, asphyxia, and in part was attributable to a direct action on the nervous centres. The autopsy showed congestion of the lungs, ecchymoses of the kidney, and much blood in the liver and spleen. Small doses of turpentine-vapour cause (according to Dr. W. B. Richardson)† giddiness, deficient appetite, and anaemia. From half an ounce to an ounce is frequently prescribed in the country as a remedy for tape-worm; in smaller quantities it is found to be a useful medicine in a great variety of ailments. The larger doses produce a kind of intoxication with giddiness, followed often by purging and strangury, not unfrequently blood or albumen (or both) is found in the urine. When in medical practice I have given the oil, and seen it given by others, in large doses for tape-worm to adults, in perhaps 40 cases, but in no one instance were the symptoms severe; the slight intoxication subsided quickly, and in a few hours the patients recovered completely. Nevertheless it has been known to destroy the lives of children, and cause most serious symptoms in adults. Two fatal cases are mentioned by Taylor; one was that of a child who died fifteen hours after taking half an ounce of the oil; in another, an infant five months old, died rapidly from a teaspoonful. The symptoms in these fatal cases were profound coma and slight convulsions; the pupils were contracted, and there was slow and irregular breathing. Turpentine is eliminated in a changed form by the kidneys, and imparts an odour of violets to the urine; but the nature of the odoriferous principle has not yet been investigated.

* Clarus in Schmidt's *Jahrbücher*, Bd. cxvii., i. 1863; and *Viertel-jahrsschr. für Ger. Med.*, xxii., Oct. 1862.

† *Brit. and For. Med.-Chir. Review*, April, 1863

II.—CAMPHOR.

A great many essential oils deposit, after exposure to air, camphors produced by oxidation of their turpenes. Ordinary camphor is imported in the rough state from China and Japan, and is prepared by distilling with water the wood of *camphora officinarum*; it is resublimed in England. The formula of camphor is $C_{10}H_{16}O$; it has a density of .896 to .996; melts at 175° , and boils at 205° . It is readily sublimed, especially in a vacuum, and is indeed so volatile at all temperatures, that a lump of camphor exposed to the air wastes away. It is somewhat insoluble in water, (about 1 part in 1,000) but this is enough to impart a distinct taste to the water; it is insoluble in chloroform, ether, acetone, acetic acid, carbon disulphide and oils. It has a fragrant colour and a burning taste. A 10 per cent. solution in alcohol turns a ray of polarised light to the right $+42.8^{\circ}$. By distillation with zinc chloride, cymene, and other products are produced. By prolonged treatment with nitric acid, camphor is oxidised to camphoric acid, ($C_{10}H_{16}O_4$). Camphor unites with bromine to form a crystalline, unstable dibromide, which splits up on distillation into hydrobromic acid and mono-brom-camphor, ($C_{10}H_{16}B_2O$). The latter is used in medicine; it crystallises in prisms fusible at 76° , and is readily soluble in alcohol.

Pharmaceutical Preparations.—The preparations officinal in the British Pharmacopœia are *camphor water*—water saturated with camphor, containing about one part per thousand.

Camphor Liniment.—A solution of camphor in olive oil, strength 25 per cent.

Compound Camphor Liniment.—Composed of camphor, oil of lavender, strong solution of ammonia and alcohol; strength in camphor about 11 per cent.

Spirit of Camphor.—A solution of camphor in spirit; strength 10 per cent.

Camphor is also a constituent of the *compound tincture of camphor*; but in this case it may be considered only a flavouring agent. There is a homœopathic solution of camphor, in spirit, (Rubini's Essence of Camphor). The solution is made by saturating alcohol with camphor; it is, therefore, very strong—about half the bulk consisting of camphor. Camphor is used in veterinary medicine both externally and internally.

Symptoms.—Camphor acts energetically on the brain and nervous system, especially if it is given in strong alcoholic solution, and thus placed under conditions favouring absorption. Some years ago Dr. G. Johnson* published a series of cases arising from the injudicious use of

* *Brit. Med. Journal*, Feb. 27, 1878, p. 272; see also *ibid*, Feb. 1875.

"homœopathic solution of camphor," from seven to forty drops of Rubini's homœopathic camphor, taken for colds, sore throat, &c., having produced coma, foaming at the mouth, convulsions, and partial paralysis. All the patients recovered, but their condition was for a little time alarming.

The cases of fatal poisoning by camphor are very rare. A woman aged 46, pregnant four months, took 12 grms. (about 184 grains) in a glass of brandy for the purpose of procuring abortion. In a very short time the symptoms commenced; she had intolerable headache, the face was flushed, and there was a sensation of burning in the stomach. In eight hours after taking the dose, she had strangury and vomiting, and the pain in the epigastrum was intense. These symptoms continued with more or less severity until the third day, when she became much worse. Her face was pale and livid, the eyes hollow, the skin cold and insensible, pulse weak and thready, breathing laboured. There were violent cramps in the stomach, and retention of urine for twenty-four hours, and then coma. The patient lingered on yet another three days, aborted, and died.*

Dr. Schaaf † has recorded three cases of poisoning—one of which was fatal. A woman gave about half a teaspoonful of a camphor solution to each of her three children, the ages being respectively five and three years and fifteen months. The symptoms noted were pallor of the face, a burning pain in the throat, thirst, vomiting, purging, convulsions, and afterwards coma. The youngest child died in seven hours; the others recovered. The smallest dose known to have produced violent symptoms in an adult is 1.3 grm. (20 grains); the largest dose known to have been recovered from is 10.2 grms. (160 grains).‡

Post-mortem Appearances.—The bodies of animals or persons dying from poisoning by camphor, smell strongly of the substance. The mucous membrane of the stomach has been found inflamed, but there seem to be no characteristic lesions.

Separation of Camphor from the Contents of the Stomach.—The identification of camphor would probably in no case present any difficulty. It may be readily dissolved out from organic fluids by chloroform. If dissolved in fixed oils, enough for the purposes of identification may be obtained by simple distillation. It is precipitated from its alcoholic solution by the addition of water.

* *Journ. de Chém.*, May, 1860.

† *Ibid.* 1850, p. 507.

‡ Taylor on "Poisons," 3rd Ed., 661.

III.—ALCOHOLS.

1. ETHYLIC ALCOHOL.

The chemical properties of ordinary alcohol are fully described, with the appropriate tests, in vol. i., "Foods," pp. 369-384, and the reader is also referred to the same volume for the composition and strength of the various alcoholic drinks.

Statistics.—If we were to include in one list the deaths indirectly due to chronic, as well as acute poisoning by alcohol, it would stand first of all poisons in order of frequency, but the taking of doses so large as to cause death in a few hours is rare. The deaths from alcohol are included by the English registrar-general under two heads—viz., those returned as dying from *delirium tremens*, and those certified as due directly to intemperance.

In the twenty-eight years from 1852-1880, the deaths certified under the head of *delirium tremens* range from the maximum number of 612 (in 1865) to the minimum of 273 (in 1879); the mean of the whole being 399 or 400 yearly. The deaths from this more acute form of alcoholic poisoning appear to be on the decrease; for if we take the five years ending 1860, out of 2,123,479 deaths from all causes, 2,361 are referred to *delirium tremens*, or 10·9 per 10,000. But in the five years ending 1880, out of 2,605,552 deaths from all causes, there were only 1,760 from *delirium tremens*, or 6·7 per 10,000. On the other hand, deaths certified as directly dependent on intemperance do not appear to have diminished, the mean number for the twenty-eight years being 426 yearly, with a minimum of 286 (in 1855), and a maximum of 777 (in 1876). While in the five years ending 1860, out of the same number of deaths as before stated, 1,492 died from intemperance, or 7·0 per 10,000; in the more recent period of five years ending 1880, 3,470 died, or 13·4 per 10,000. In Sweden, as well as in Russia, the mortality from alcohol is greater than in this country; whilst in the warmer climates it becomes insignificant as a cause of death.*

Criminal or Accidental Alcoholic Poisoning.—Suicide by alcohol in the common acceptance of the term, is rare, and murder still rarer, though not unknown. Perhaps the most common cause of fatal acute poisoning by alcohol is either a foolish wager, by which a man bets that he can drink so many glasses of spirits without bad effect; or else the

* "Drunkenness as Modified by Race," is the title of an interesting paper by Dr. Druitt. (*Med. Times and Gaz.*, April 15, 1872). It is summarised with other facts in the present writer's "Dictionary of Hygiène," art. "Alcohol."

drugging of a person already drunk by his companions in a sportive spirit.

Fatal Dose.—It is difficult to say what would be likely to prove a lethal dose of alcohol, for a great deal depends without doubt on the dilution of the spirit, since the mere local action of strong alcohol on the mucous membranes of the stomach, &c., is severe (one may almost say corrosive), and would aid the more remote effects. In Maschka's case,* a boy of nine years and a girl of five, died from about two and a half ounces of spirit of 67 per cent. strength, or 48.2 cc. (1.7 oz.) of absolute alcohol.

In a case related by Taylor, a child seven years old died from some quantity of brandy, probably about 113.4 cc. (4 oz), which will be equal to at least 56.7 cc. (2 oz.) of absolute alcohol. From other cases in which the quantity of absolute alcohol can be, with some approximation to the truth, valued, it is evident, that for any child below ten or twelve, quantities of from 28.3 to 56.6 cc. (1-2 oz.) of absolute alcohol contained in brandy, gin, &c., would be a highly dangerous and probably fatal dose—while the toxic dose for adults is somewhere between 71.8-141.7 cc. (2.5-5 oz.).

Symptoms.—In the cases of rapid poisoning by a large dose of alcohol, which alone concern us, the preliminary, and too familiar excitement of the drunkard, may be hardly observable; but the second stage, that of depression, rapidly sets in; the unhappy victim sinks down to the ground helpless, the face pale, the eyes injected and staring, the pupils dilated, acting sluggishly to light, and the skin remarkably cold.

* Recorded by Maschka (*Gutachten der Prager Facultät*, iv., 239, see also Maschka's "Handbuch der Gericht. Medicin," Band. ii., p. 384). The following is a brief summary:—Franz. Z., nine years old, and Caroline Z., eight years old, were poisoned by their stepfather with spirit of 67 per cent. strength taken in small quantities by each—at first by persuasion and the remainder administered by force. About one-eighth of a pint is said to have been given to each child. Both vomited somewhat, then lying down, stertorous breathing at once came on, and they quickly died. The autopsy, three days after death, showed dilatation of the pupils; *rigor mortis* present in the boy, not in the girl; and the membranes of the brain filled with dark fluid blood. The smell of alcohol was perceptible on opening the chest; the mucous membrane of the bronchial tubes and gullet was normal, both lungs oedematous, the fine tubes gorged with a bloody frothy fluid, and the mucous membrane of the whole intestinal canal was reddened. The stomach was not, unfortunately, examined, being reserved for chemical analysis. The heart was healthy; the pericardium contained some straw-coloured fluid. Chemical analysis gave an entirely negative result, which must have been from insufficient material having been submitted to the analyst, for I cannot see how the vapours of alcohol could have been detected by the smell, and yet have evaded chemical processes.

Fräntzel* found, in a case in which the patient survived, a temperature of only 24.6° in the rectum, and in that of another person who died, a temperature of 23.8°. The mucous membranes are of a peculiar dusky blue; the pulse, which at first is quick, soon becomes slow and small; the respiration is also slowed, intermittent, and stertorous; there is complete loss of consciousness and motion; the breath smells strongly of the alcoholic drink, and if the coma continues there may be vomiting and involuntary passing of excreta. Death ultimately occurs through paralysis of the respiratory centres. Convulsions in adults are rare, in children frequent. Death has more than once been immediately caused, not by the poison, but by accidents dependent upon loss of consciousness. Thus food has been sucked into the air-tubes, or the person has fallen, so that the face was buried in water, ordure, or mud; here suffocation has been induced by mechanical causes.

A remarkable course not known with any other narcotic is that in which the symptoms remit, the person wakes up, as it were, moves about and does one or more rational acts and then suddenly dies. In this case also, the death is not directly due to alcohol, but indirectly—the alcohol having developed œdema, pneumonia, or other affection of the lungs, which causes the sudden termination when the first effect of the poison has gone off. The time that may elapse from the commencement of coma till death varies from a few minutes to days; death has occurred after a quarter of an hour, half an hour, and an hour. It has also been prolonged to three, four, and six days, during the whole of which the coma has continued. The average period may, however, be put at from six to ten hours.

Post-mortem Appearances.—Cadaveric rigidity lasts tolerably long. Casper has seen it still existing nine days after death, and Seidel† seven days (in February). Putrefaction is retarded in those cases, in which a very large dose has been taken, but this is not a very noticeable or constant characteristic. The pupils are mostly dilated. The smell of alcohol should be watched for, but it will only be present in cases where but a short time has elapsed between the taking of the poison and death; putrefaction may also conceal it. Under favourable circumstances, especially if the weather is cold, the alcoholic smell may remain a long time. Alcohol may cause the most intense redness and congestion of the stomach. The most inflamed stomach I ever saw, short of inflammation by the corrosive poisons, was that of a sailor, who died suddenly after a twenty-four hours' drinking bout; all the organs of the body were fairly healthy, the man had suffered from no disease; analysis

* *Temperaturerniedrigung durch Alcoholintoxication, Charité Annalen*, i., 371.

† Seidel, *Maschka's Handbuch*, Bd. ii., p. 380.

could detect no poison but alcohol ; and the history of the case, moreover, proved clearly that it was a pure case of alcoholic poisoning.

In a case related by Taylor, in which a child drank four ounces of brandy and died, the mucous membrane of the stomach presented patches of intense redness, and in several places was thickened and softened, some portions being actually detached and hanging loose, and there were evident signs of extravasations of blood. The effect may not be confined to the stomach, but extend to the duodenum and even to the whole intestinal canal. The blood is generally dark and fluid, and usually the contents of the skull are markedly hyperæmic, the pia very full of blood, the sinuses and plexus gorged ; occasionally, the brain-substance shows signs of unusual congestion ; serum is often found in the ventricles. The great veins of the neck, the lungs, and the right side of the heart, are very often found full of blood, and the left side empty. Oedema of the lungs also occurs with tolerable frequency. The great veins of the abdomen are also filled with blood, and if the coma has been prolonged without surgical aid, the bladder will be distended with urine. A rare phenomenon has been also noticed—namely, the occurrence of blebs on the extremities, &c., just as if the part affected had been burnt or scalded. Lastly, with the changes directly due to the fatal dose may be included all those degenerations met with in the chronic drinker, provided the case had a history of previous intemperance.

Excretion of Alcohol.—Alcohol, in the diluted form, is quickly absorbed by the blood-vessels of the stomach, &c., and circulates in the blood ; but what becomes of it afterwards is by no means settled. I think there can be little doubt that the lungs are the main channels through which it is eliminated ; with persons given up to habits of intemperance, the breath has constantly a very peculiar ethereal odour, probably dependent upon some highly volatile oxidised product of alcohol.

Alcohol is eliminated in small proportion only by the kidneys Thudichum, in an experiment* by which 4,000 grms. of absolute alcohol were consumed by thirty-three men, could only find in the collected urine 10 grms. of alcohol. The numerous experiments by Dupré also establish the same truth, that but a fraction of the total alcohol absorbed is excreted by the kidneys. According to Lallemand, Perrin, and Duroy, the content of the brain in alcohol is more than that of the other organs. I have found also that the brain after death has a wonderful attraction for alcohol, and yields it up at a water-heat very slowly and with difficulty. In one experiment, in which a finely-divided portion of brain, which had been soaking in alcohol for many weeks, was submitted to a steam

* See Thudichum's "Pathology of the Urine," London, 1877, in which both his own and Dr. Dupré's experiments are summarised.

heat of 100° , twenty-four hours' consecutive heating failed to expel every trace of spirit.

It is probable that true alcoholates of the chemical constituents of the brain are formed. In the case of vegetable colloidal bodies, such, for example, as the pulp of cherries, a similar attraction has been observed, the fruit condensing, as it were, the alcohol in its own tissues, and the outer liquid being of less alcoholic strength than that which can be expressed from the steeped cherries. Alcohol is also excreted by the sweat, and minute fractions have been found in the faeces.

Toxicological Detection of Alcohol.—(see vol. i., "Foods," 369-384). The living cells of the body produce minute quantities of alcohol, and it is often found in traces in putrefying fluids. Hence, mere qualitative proofs of the presence of alcohol are insufficient on which to base an opinion as to whether alcohol had been taken during life or not, and it will be necessary to estimate the quantity accurately by some of the processes detailed in vol. i., p. 373, *et seq.* In those cases in which alcohol is found in quantity in the stomach, there can, of course, be no difficulty; in others, the whole of the alcohol may have been absorbed, and chemical evidence, unless extremely definite, must be supplemented by other facts.

2. AMYLC ALCOHOL.

Amylic Alcohol.—*Formula* ($C_5H_{11}HO$).—There is more than one amylic alcohol. The amylic alcohols are identical in their chemical composition, but differ in certain physical properties, normal amylic alcohol boiling at 135° , and iso-amyl alcohol at from $128-132^{\circ}$. The latter has a specific gravity of .8148, and is the variety produced by fermentation and present in fusel oil.

The experiments of Eulenberg* on rabbits, Cross † on pigeons, Rabuteau ‡ on frogs, and Furst on rabbits, with those of Dr. W. B. Richardson § on various animals, have shown it to be a powerful poison, more especially if breathed in a state of vapour.

Dr. Richardson, as the result of his investigations, considers that

* *Gewerbe Hygiène.* 1876, p. 440.

† *De l'Alcohol Amylique et Methyl sur l'Organisme. Thèse.* Strasburg, 1863.

‡ *Ueber die Wirkung des Aethyl, Butyl u. Amyl Alcohols.* *L'Union.* Nos. 90, 91, 1870. *Schmidts Jahrb.* Bd. 149, p. 263.

§ *Trans. Brit. Association*, 1864, 1865, and 1866. Also *Brit. and Foreign Med. Chir. Rev.* Jan. 7, 1867, p. 247.

amyl alcohol when breathed sets up quite a peculiar class of symptoms which last for many hours, and are of such a character, that it might be thought impossible for the animal to recover, although they have not yet been known to prove fatal. There is muscular paralysis with paroxysms of tremulous convulsions; the spasms are excited by touching the animal, breathing upon it, or otherwise subjecting it to trifling excitation.

Hitherto, neither the impure fusel oil, nor the purer chemical preparation has had any toxicological importance. Should it be necessary at any time to recover small quantities from organic liquids, the easiest way is to shake the liquid up with chloroform, which readily dissolves amylic alcohol, and on evaporation leaves it in a state pure enough to be identified. Amyl alcohol is identified by the following tests:—(1.) Its physical properties; (2.) If warmed with twice its volume of strong sulphuric acid, a rose or red colour is produced; (3.) Heated with an acetate and strong sulphuric acid, *amyl acetate*, which has the odour of the jargonelle pear, is formed; (4.) Heated with sulphuric acid and potassic dichromate, valeric aldehyde is first produced, and then valeric acid is formed; the latter has a most peculiar and strong odour.

Amyl Nitrite, ($C_5H_{11}NO_2$).—Boiling point 95° to 100° , specific gravity .877. Amyl nitrite is a limpid, and, generally, slightly yellow liquid; it has a peculiar and characteristic odour. On heating with alcoholic potash, the products are nitrite of potash and amylic alcohol; the amylic alcohol may be distilled off and identified. The presence of a nitrite in the alkaline solution is readily shown by the colour produced, by adding a few drops of a solution of meta-phenylene-diamine.

Dr. B. W. Richardson and others have investigated the action of amyl nitrite, as well as that of the acetate and iodide; they all act in a similar manner, the nitrite being most potent. After absorption, the effects of amyl nitrite are especially seen on the heart and circulation; the heart acts violently, there is first dilatation of the capillaries, then this is followed by diminished action of the heart and contraction of the capillaries.

According to Dr Richardson, it suspends the animation of frogs. No other substance known will thus suspend a frog's animation for so long a time without killing it. Under favourable circumstances, the animal will remain apparently dead for many days, and yet recover. Warm-blooded animals may be thrown by amylic alcohol into a cataleptic condition. It is not an anæsthetic, and by its use consciousness is not destroyed, unless a condition approaching death be first produced. When this occurs there is rarely recovery; the animal passes into actual death.

Post-mortem Appearances.—If administered quickly, the lungs and all the other organs are found blanched and free from blood, the right side of the heart gorged with blood, the left empty, the brain being free from congestion. If administered slowly, the brain is found congested, and there is blood both on the left and right sides of the heart.

IV.—ETHER.

Ether, Ethylic Ether, Ethyl Oxide, $(C_2H_5)_2O$.—Ethylic ether is a highly mobile liquid of peculiar penetrating odour and sweetish pungent taste. It is perfectly colourless, and evaporates so rapidly, that when applied in the form of spray to the skin, the latter becomes frozen, and is thus deprived of sensibility.

Pure ether has a density of .713, its boiling point is 35° , but commercial samples, which often contain water, (one part of water is soluble in thirty-five of ether), may have a higher gravity, and also a higher boiling point. The readiest way to know whether an ether is anhydrous or not, is to shake it up with a little carbon disulphide. If it is hydrous, the mixture is milky. Methylated ether is largely used in commerce; its disagreeable odour is due to contamination by methylated compounds; otherwise the ether made from methylated spirit is ethylic ether, for methylic ether is a gas which escapes during the process. Hence the term "methylated" ether is misleading, for it contains no methylic ether, but is essentially a somewhat impure ethylic ether.

Ether as a Poison.—Ether has but little toxicological importance. There are a few cases of death from its use as an anaesthetic, and a few cases of suicide. Ether is used by some people as a stimulant, but ether drinkers are uncommon. It causes an intoxication very similar to that of alcohol, but of brief duration. In a case of chronic ether-taking recorded by Martin,* in which a woman took daily doses of ether for the purpose of allaying a gastric trouble, the patient suffered from shivering or trembling of the hands and feet, muscular weakness, cramp in the calves of the legs, pain in the breast and back, intermittent headaches, palpitation, singing in the ears, vomitings and wakefulness; the ether being discontinued, the patient recovered. In one of Orfila's experiments, half an ounce of ether was administered to a dog. The animal died insensible in three hours. The mucous membrane of the stomach was found highly inflamed, the inflammation extending somewhat into the duodenum; the rest of the canal was healthy. The lungs were gorged with fluid blood.

Fatal Dose.—The fatal dose of ether, when taken as a liquid, is not known. 4 grms. (1.28 drms.) cause toxic symptoms, but the effect soon passes. Buchanan has seen a brandy-drinker consume 25 grms. (6.4 drms.) and yet survive. It is probable that most adults would be killed by a fluid ounce (28.4 cc.)

Ether as an Anaesthetic.—Ether is now much used as an anaesthetic,

* Virchow's *Jahresber.*, 1870.

and generally in conjunction with chloroform. Anæsthesia by ether is said to compare favourably with that induced by chloroform. In 92,000 cases of operations performed under ether, the proportion dying from the effects of the anaesthetic was only 3 per 10,000 (Morgan), while chloroform gives a higher number (see p. 129). The mortality in America, again, from a mixture of chloroform and ether in 11,000 cases is reckoned at 1.7 per 10,000; but this proportion is rather above some of the calculations relative to the mortality from pure chloroform, so that the question can hardly be considered settled. The symptoms of ether narcosis are very similar to those produced by chloroform. The chief point of difference appears to be its action on the heart. Ether, when first breathed, stimulates the heart's action, and the after-depression that follows never reaches so high a grade as with chloroform. Ether is said to kill by paralysing the respiration, and in cases which end fatally the breathing is seen to stop suddenly: convulsions have not been noticed. The *post-mortem* appearances, as in the case of chloroform, are not characteristic.

Separation of Ether from Organic Fluids, &c.—Despite the low boiling point of ether, it is by no means easy to separate it from organic substances *so as to recover the whole of the ether present*. The best way is to place the matters in a flask connected with an ordinary Liebig's condenser, the tube of the latter at its farther end fitting closely into the doubly-perforated cork of a flask. Into the second perforation is adapted an upright tube about two feet long, which may be of small diameter, and must be surrounded by a freezing mixture of ice and salt. The upper end of this tube is closed by a thistle-head funnel with syphon, and in the bend of the syphon a little mercury serves as a valve. Heat is now applied to the flask by means of a water-bath, and continued for several hours; the liquid which has distilled over is then treated with dry calcic chloride and redistilled exactly in the same way. To this distillate again a similar process may be used, substituting dry potassic carbonate for the calcic chloride. It is only by operating on these principles that the expert can recover in an approximate state of anhydrous purity such a volatile liquid. Having thus obtained it pure, it may be identified (1) by its smell, (2) by its boiling point, (3) by its inflammability, and (4) by its reducing chromic acid; the latter test may be applied to the vapour. An asbestos fibre is soaked in a mixture of strong sulphuric acid and potassic dichromate, and then placed in the tube connected with the flask—the ethereal (or alcoholic) vapour passing over the fibre, immediately reduces the chromic acid to chromic oxide, with the production of a green colour.

V.—CHLOROFORM.

CHLOROFORM, TRICHLOROMETHANE OR METHENYL CHLORIDE. •
(CHCl_3).

Chloroform appears to have been discovered independently by Soubeiran and Liebig, about 1830. It was first employed in medicine by Simpson, of Edinburgh, as an anaesthetic. Pure chloroform has a density of 1.491 at 17° and boils at 60.8°; but commercial samples have gravities of from 1.47 to 1.491. It is a colourless liquid, strongly refracting light; it cannot be ignited by itself, but, when mixed with alcohol, burns with a smoky flame edged with green. Its odour is heavy, but rather pleasant; the taste is sweet and burning.

Chloroform sinks in water, and is only slightly soluble in that fluid (·44 in 100 cc.); it is perfectly neutral in reaction, and very volatile. When rubbed on the skin it should completely evaporate, leaving no odour. Pure absolute chloroform gives an opaline mixture if mixed with from one to five volumes of alcohol, but with any quantity above five volumes the mixture is clear; it mixes in all proportions with ether. Chloroform coagulates albumen, and is an excellent solvent for most organic bases—camphor, caoutchouc, amber, opal, and all common resins. It dissolves phosphorus and sulphur slightly,—more freely iodine and bromine. It floats on hydric sulphate, which only attacks it at a boiling heat.

Chloroform is not unfrequently adulterated, or (perhaps a better term would be) made impure from faulty manufacture. The impurities to be sought are alcohol, methylated chloroform,* dichloride of ethylene, ($\text{C}_2\text{H}_4\text{Cl}_2$), chloride of ethyl, ($\text{C}_2\text{H}_5\text{Cl}$), aldehyde, chlorine, hydrochloric, hypochlorous, and traces of sulphuric acid; there have also been found chlorinated oils. One of the best tests for contamination by alcohol, wood spirit, or ether, is that known as Roussin's; dinitrosulphide of iron † is added to chloroform. If it contain any of these impurities, it acquires a dark colour, but if pure, remains bright and colourless.

The presence of alcohol or ether, or both, may also be discovered by the bichromate test, which is best applied as follows:—A few milli-

* Methylated chloroform is that which is prepared from methylated spirit. It is liable to more impurities than that made from pure alcohol, but, of course, its composition is the same, and it has recently been manufactured from this source almost chemically pure.

† Made by slowly adding ferric sulphate to a boiling solution of ammonic sulphide and potassic nitrite, as long as the precipitate continues to redissolve, and then filtering the solution.

grammes of potassic bichromate are placed at the bottom of a test-tube with four or five drops of sulphuric acid, which liberates the chromic acid ; next, a very little water is added to dissolve the chromic acid ; and lastly, the chloroform. The whole is now shaken, and allowed to separate. If the chloroform is pure, the mass is hardly tinged a greenish-yellow, and no layer separates. If, however, there is anything like 5 per cent. of alcohol or ether present, the deep green of chromium chloride appears, and there is a distinct layer at the bottom of the tube.

Another way to detect alcohol in chloroform, and also to make an approximate estimation of its quantity, is to place 20 cc. of chloroform in a burette, and then add 80 cc. of water. On shaking violently, pure chloroform will sink to the bottom in clear globules, and the measurement will be as nearly as possible the original quantity ; but if anything like a percentage of alcohol be present, the chloroform is seen to be diminished in quantity, and its surface is opalescent, the diminution being caused by the water dissolving out the alcohol. The addition of a few drops of potash solution destroys the meniscus, and allows of a close reading of the volume. The supernatant water may be utilised for the detection of other impurities, and tested for sulphuric acid by baric chloride, for free chlorine and hypochlorous acid by starch and potassic iodide, and for hydrochloric acid by silver nitrate.* Fuchsine, proposed by Stödeler, is also a delicate reagent for the presence of alcohol in chloroform, the sample becoming red in the presence of alcohol, and the tint being proportionate to the quantity present. The most delicate test for alcohol is, however, the iodoform test fully described in vol. i., "Foods," p. 375,† Dichloride of ethylene is detected by shaking up the chloroform with dry potassic carbonate, and then adding metallic potassium. This does not act on pure chloroform, but only in presence of ethylene dichloride, when the gaseous chlor-ethylene (C_2H_5Cl) is evolved. Ethyl-chloride is detected by distilling the chloroform and collecting the first portions of the distillate ; it will have a distinct odour of ethyl-chloride should it be present. Methyl compounds and empyreumatic oils are roughly detected by allowing the chloroform to evaporate on a cloth. If present, the cloth, when the chloroform has evaporated, will have a peculiar disagreeable odour. Aldehyde is recognised by its reducing action on argentic nitrate ; the mineral acids by the reddening of litmus paper,

* Neither an alcoholic nor an aqueous solution of silver nitrate causes the slightest change in pure chloroform.

† An attempt has been made by Besnou to estimate the amount of alcohol by the specific gravity. He found that a chloroform of 1.4945 gravity, mixed with 5 per cent. of alcohol, gave a specific gravity of 1.4772 ; 10 per cent., 1.4602 ; 20 per cent., 1.4262 ; and 25 per cent., 1.4090. It would, therefore, seem that every percentage of alcohol lowers the gravity by .0084.

and the appropriate tests. Hypochlorous acid first reddens, and then bleaches, litmus paper.

The ordinary method of manufacturing chloroform is by distilling alcohol with chlorinated lime ; but another mode is now much in use—viz., the decomposition of chloral hydrate. By distilling it with a weak alkali, this process yields such a pure chloroform, that, for medical purposes, it should supersede every other.

POISONOUS EFFECTS OF CHLOROFORM.

1. *As a Liquid.*

Statistics.—Falck finds recorded in medical literature twenty-seven cases of poisoning by chloroform having been swallowed—of these fifteen were men, nine were women, and three children. Eighteen of the cases were suicidal, and ten of the eighteen died ; the remainder took the liquid by mistake.

Local Action of Chloroform.—When applied to the skin or mucous membranes in such a way that the fluid cannot evaporate—as, for example, by means of a cloth steeped in chloroform laid on the bare skin, and covered over with some impervious material—there is a burning sensation, which soon ceases, and leaves the part anæsthetised, while the skin, at the same time, is reddened and sometimes even blistered.

Chloroform added to blood, or passed through it in the state of vapour, causes it to assume a peculiar brownish colour, owing to destruction of the red corpuscles and solution of the haemoglobin in the plasma. The change does not require the presence of atmospheric air, but takes place equally in an atmosphere of hydrogen. It has been shown by Schmiedeberg that the chloroform enters in some way into a state of combination with the blood-corpuscles, for the entire quantity cannot be recovered by distillation ; whereas the plasma, similarly treated, yields the entire quantity which has in the first place been added. S. Schmiedeberg also asserts that the oxygen is in firmer combination with the chloroformised blood than usual, as shown by its slow extraction by stannous oxide. Muscle, exposed to chloroform liquid by arterial injection, quickly loses excitability and becomes rigid. Nerves are first stimulated, and then their function for the time is annihilated ; but on evaporation of the chloroform, the function is restored.

General Effects of the Liquid.—However poisonous in a state of vapour, chloroform cannot be considered an extremely active poison when taken into the stomach as a liquid, for enormous quantities, relatively, have been drunk without fatal effect. Thus, there is the case recorded

by Taylor, in which a man, who had swallowed 118·4 grms. (4 oz.), walked a considerable distance after taking the dose. He subsequently fell into a state of coma, with dilated pupils, stertorous breathing, and imperceptible pulse. These symptoms were followed by convulsions, but the patient recovered in five days.

In a case related by Burkart,* a woman desired to kill herself with chloroform, and procured for that purpose 50 grms. (a little more than one ounce and a half); she drank some of it, but the burning taste and the sense of heat in the mouth, throat, and stomach, prevented her from taking the whole at once. After a few moments, the pain passing off, she essayed to drink the remainder, and did swallow the greater portion of it, but was again prevented by the suffering it caused. Finally, she poured what remained on a cloth, and placing it over her face, soon sank into a deep narcosis. She was found lying on the bed very pale, with blue lips, and foaming a little at the mouth; the head was rigidly bent backwards, the extremities were lax, the eyes were turned upwards and inwards, the pupils dilated and inactive, the face and extremities were cold, the body somewhat warmer, there was no pulse at the wrist, the carotids beat feebly, the breathing was deep and rattling, and after five or six inspirations ceased. By the aid of artificial respiration, &c., she recovered in an hour.

A still larger dose has been recovered from in the case of a young man, aged twenty-three,† who had swallowed no less than 75 grms. (2½ ounces) of chloroform, but yet, in a few hours, awoke from the stupor. He complained of a burning pain in the stomach; on the following day he suffered from vomiting, and on the third day symptoms of jaundice appeared,—a feature which has been several times noticed as an effect of chloroform.

On the other hand, even small doses have been known to destroy life. In a case related by Taylor, a boy, aged four, swallowed 3·8 grm. (1 drachm) of chloroform and died in three hours, notwithstanding that every effort was used for his recovery.

The smallest dose that has proved fatal to an adult is 15 grms. (nearly 4 drachms).

From twenty-two cases in which the quantity taken had been ascertained with some degree of accuracy, Falck draws the following conclusions:—In eight of the cases the dose was between 4 and 30 grms., and one death resulted from 15 grms. As for the other fourteen persons, the doses varied from 35 to 380 grms., and eight of these patients died—two after 40, two after 45, one after 60, 90, 120 and 180 grms. re-

* *Vierteljahrsschr. für Ger. Med.*, 1878.

† *Brit. Med. Journ.*, 1879.

spectively. Hence, under conditions favouring the action of the poison, 15 grms. (3·8 drachms) may be fatal to an adult, while doses of 40 grms. (10·3 drachms) and upwards, will almost certainly kill.

Symptoms.—The symptoms can be well gathered from the cases quoted. They commence shortly after the taking of the poison; and, indeed, the local action of the liquid immediately causes first a burning sensation, followed by numbness.

Often after a few minutes, precisely as when the vapour is administered, a peculiar, excited condition supervenes, accompanied, it may be, by delirium. The next stage is narcosis, and the patient lies with pale face and livid lips, &c., as described at p. 131; the end of the scene is often preceded by convulsions. Sometimes, however, consciousness returns, and the irritation of the mucous membranes of the gastro-intestinal canal is shown by bloody vomiting and bloody stools, with considerable pain and general suffering. In this way, a person may linger several days after the ingestion of the poison. In a case observed by Pomeroy, the fatal malady was prolonged for eight days. Among those who recover, a common *sæquela*, as before mentioned, is jaundice.

A third form of symptoms has been occasionally observed, viz.:—the person awakes from the coma, the breathing and pulse become again natural, and all danger seems to have passed, when suddenly, after a longer or shorter time, without warning, a state of general depression and collapse supervenes, and death occurs.

Post-mortem Appearances.—The *post-mortem* appearances from a fatal dose of liquid chloroform mainly resolve themselves into redness of the mucous membrane of the stomach, though occasionally, as in Pomeroy's case, there may be an ulceration. In a case recorded by Hoffman,* a woman, aged thirty, drank 35 to 40 grms. of chloroform and died within the hour. Almost the whole of the chloroform taken was found in the stomach, as a heavy fluid, coloured green, through the bile. The epithelium of the pharynx, epiglottis, and gullet, was of a dirty colour, partly detached, whitened, softened, and easily stripped off. The mucous membrane of the stomach was much altered in colour and consistence, and, with the duodenum, was covered with a tenacious grey slime. There was no ecchymosis.

The Vapour of Chloroform.

Accidents occur far more frequently in the use of chloroform vapour for anaesthetic purposes than in use of the liquid.

Statistics.—Most of the cases of deaths through chloroform-vapour, are those caused accidentally in surgical and medical practice. A smaller

* *Lehrbuch der Ger. Medicin*, 2te Aufl.

number are suicidal, while for criminal purposes its use is extremely infrequent.

The percentage of deaths caused by chloroform administered during operations, is unaccountably different in different years, times, and places. The diversity of opinion on the subject is partly (though not entirely) explicable, by the degrees of purity in the anæsthetic administered, the different modes of administration, the varying lengths of time of the anæsthesia, and the varying severity of the operations.

During the Crimean war, according to Baudens and Quesnoy, 30,000 operations were done under chloroform, but only one death occurred attributable to the anæsthetic. Sansom* puts the average mortality at .75 per 10,000, Nussbaum at 1.3, Richardson at 2.8 † Morgan ‡ at 3.4. In the American war of secession in 11,000 operations, there were seven deaths—that is 6.3 per 10,000, the highest number on a large scale which appears to be on record.

Suicidal and Criminal Poisoning by Chloroform.—Suicidal poisoning by chloroform will generally be indicated by the surrounding circumstances; and in no case hitherto reported has there been any difficulty or obscurity as to whether the narcosis was self-induced or not. An interesting case is related by Schanenstein, § in which a physician resolved to commit suicide by chloroform, a commencing amaurosis having preyed upon his mind, and his choice having been determined by witnessing an accidental death by this agent. He accordingly plugged his nostrils, fitted on to the face an appropriate mask, and fastened it by strips of adhesive plaster. In such an instance, there could be no doubt of the suicidal intent, and the question of accident would be entirely out of the question.

A dentist in Potsdam, || in a state of great mental depression from embarrassed circumstances, killed his wife, himself, and two children by chloroform. Such crimes are fortunately very rare.

There is a vulgar idea that it is possible, by holding a cloth saturated with chloroform to the mouth of a sleeping person (or one, indeed, perfectly awake), to produce a *sudden* insensibility; but such an occurrence is against all experimental and clinical evidence. It is true that a nervous person might, under such circumstances, faint and become insensible by mere nervous shock; but a true sudden narcosis is impossible.

Dolbeau has made some interesting experiments in order to ascertain

* "Chloroform: its Action, &c.," London, 1865.

† *Med. Times and Gazette*, 1870.

‡ *Med. Soc. of Virginia*, 1872.

§ Maschka: *Handbuch der Gerichtlich. Medicin*, p. 787. Tübingen, 1882.

|| Casper: *Handbuch der Ger. Med.*

whether under any circumstances a sleeping person might be anaesthetised. The main result appears to answer the question in the affirmative, at least with certain persons; but even with these it can only be done by using the greatest skill and care, first allowing the sleeper to breathe very dilute chloroform-vapour, and then gradually exhibiting stronger doses, and taking the cloth or inhaler away on the slightest symptom of approaching wakefulness. In 75 per cent. of the cases, however, the individuals awoke almost immediately on being exposed to the vapour. This cautious and scientific narcosis, then, is not likely to be used by the criminal class, or, if used, to be successful.

Symptoms.—There is but little outward difference between man and animals, in regard to the symptoms caused by breathing chloroform; in the former we have the advantage that the sensations preceding narcosis can be described by the individual.

The action of chloroform is usually divided into three more or less distinct stages. In the *first* there is a "drunken" condition, changes in the sense of smell and taste, and it may be hallucinations of vision and hearing; there are also often curious creeping sensations about the skin, and sometimes excessive muscular action, causing violent struggles. I have also seen epileptiform convulsions, and delirium is almost always present. The face during this stage is generally flushed, covered with perspiration, and the pupils contracted. The first stage may last from one minute to several, and then pass into the *second stage*, or that of depression. Spontaneous movements cease, sensibility to all external stimuli vanishes, the patient falls into a deep sleep, the consciousness is entirely lost, and reflex movements are more and more annihilated. The temperature is less than normal, the respirations are slow, and the pulse is full and slow. The pupils in this stage are usually dilated, all the muscles are relaxed, and the limbs can be bent about in any direction. If now the inhalation of chloroform is intermittent, the patient wakes within a period which is usually from twenty to forty minutes, but may be several hours after the last inhalation.

The *third stage* is that of paralysis; the pulse becomes irregular, the respirations superficial, there is a cyanotic colouring of the lips and skin, while the pupils become widely dilated. Death follows quickly through paralysis of the heart or respiratory centres.

According to Sansom's facts,* in 100 cases of death by chloroform, 44.6 per cent. occurred before the full narcosis had been attained, that is in the first stage, 34.7 during the second stage, and 20.6 shortly after. So, also, Kappeler has recorded that in 101 cases of death from chloroform, 47.7 per cent. occurred before the full effect, and 52.2 during the full effect. This confirms the dictum of Billroth, that in all stages of

* *Op. Cit.*

anæsthesia by chloroform, death may occur. The quantity of chloroform, which, when inhaled in a given time, will produce death, is unknown, for all depends upon the greater or less admixture of air, and probably on other conditions. It has been laid down, that the inhalation of chloroform should be so managed as to insure that the air breathed shall never contain more than 3·9 per cent. of chloroform. Fifteen drops have caused death, but Taylor, on the other hand, records a case of tetanus, treated at Guy's Hospital, in which no less a quantity than 700 grms. (22·5 oz.) was inhaled in twenty-four hours. Frequent breathing of chloroform in no way renders the individual safe from fatal accident. A lady* having repeatedly taken chloroform, was anaesthetised by the same agent merely for the purpose of having a tooth extracted. About 6 grms. (1·5 drm.) were poured on a cloth, and after nine to ten inspirations, dangerous symptoms began—rattling breathing and convulsive movements—and, despite all remedies, she died.

Chronic chloroform poisoning is not unknown. It leads to various ailments, and seems to have been in one or two instances the cause of insanity.

Buchner records the case of an opium-eater, who afterwards took to chloroform; he suffered from periodic mania. In a remarkable case related by Meric, the patient, who had also first been a morphine eater, took 350 grms. of chloroform in five days by inhalation; as often as he woke he would chloroform himself again to sleep. In this case, there was also mental disturbance, and instances in which chloroform produced marked mental aberration are recorded by Böhm† and by Vigla.‡

Post-Mortem Appearances.—The lesions found on section are neither peculiar to, nor characteristic of, chloroform poison. It has been noted that bubbles of gas are, from time to time, to be observed after death in the blood of those poisoned by chloroform, but it is doubtful whether the bubbles are not merely those to be found in any other corpse—in 189 cases, only eighteen times were these gas-bubbles observed,§ so that, even if they are characteristic, the chances in a given case that they will not be seen are greater than the reverse. The smell of chloroform may be present, but has been noticed very seldom.

The Detection and Estimation of Chloroform from organic substances is not difficult, its low boiling point causing it to distil readily. Accordingly (whatever may be the ultimate modifications as suggested by different experimenters) the first step is to bring the substances, unless fluid, into a pulp with water, and submit this pulp to distillation by the

* *Edin. Med. Journ.*, 1855

† *Ziemssen's Handbuch.* Bd. 15.

‡ *Med. Times*, 1855.

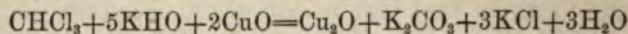
§ *Schaunenstein, (Op. cit.)*

heat of a water-bath. If the liquid operated upon possesses no particular odour, the chloroform may in this way be recognised in the distillate, which, if necessary, may be redistilled in the same manner, so as to concentrate the volatile matters in a small compass.

There are four chief tests for the identification of chloroform:—

(1.) The final distillate is tested with a little aniline and an alcoholic solution of soda lye; either immediately, or upon gently warming the liquid, there is a peculiar and penetrating odour of benzo-iso-nitrile (C_7H_5N). Chloral, trichloracetic acid, bromoform and idoform also give the same reaction; on the other hand, ethylidene chloride does not yield under these circumstances any isonitile.

(2.) Chloroform reduces Fehling's alkaline copper solution, *when applied to a distillate*, thus excluding a host of more fixed bodies which have the same reaction; it is a very excellent test, and may be made quantitative. The reaction is as follows:—



thus, every 100 parts of cuprous oxide equals 88.56 of chloroform.

(3.) The fluid to be tested (which, if acid, should be neutralised), is distilled in a slow current of hydrogen, and the vapour conducted through a short bit of red-hot combustion-tube containing platinum gauze. Under these circumstances, the chloroform is decomposed and hydrochloric acid formed; hence, the issuing vapour has an acid reaction to test paper, and if led into a solution of silver nitrate, gives the usual precipitate of argentic chloride. Every 100 parts of silver chloride equal 27.758 of chloroform.

(4.) The fluid is mixed with a little thymol and potash; if chloroform be present, a reddish-violet colour is developed, becoming more distinct on the application of heat.*

For the quantitative estimation of chloroform the method recommended by Schmiedeberg† is, however, the best. A combustion-tube of 24 to 26 cm. long, and 10 to 12 mm. in diameter, open at both ends, and made of glass fusible with difficulty, is furnished at the one end with a plug of asbestos, while the middle part, to within 5-6 cm. of the other end, is filled with pieces of caustic lime, from the size of a lentil to that of half a pea. The lime must be pure, and is made from heating a carbonate which has been precipitated from calcic nitrate. The other end of the tube is closed by a cork, carrying a silver tube, 16-18. cm. long, and

* S. Vidali in *Deutsch-Amerikan. Apoth.-Zeitung*, vol. iij., Aug. 15, 1882.

† *Ueber die quantitative Bestimmung des Chloroforms in Blute.* Inaug. Dissert., Dorpat, 1866.

4 mm. thick. The end containing the asbestos plug is fitted by a cork to a glass tube. The combustion-tube thus prepared is placed in the ordinary combustion-furnace ; the flask containing the chloroform is adapted, and the distillation slowly proceeded with. It is best to add a tube, bent at right angles and going to the bottom of the flask, to draw air continuously through the apparatus. During the whole process, the tube containing lime is kept at a red heat. The chloroform is decomposed, and the chlorine combines with the lime. The resulting calcic chloride, mixed with much unchanged lime, is, at the end of the operation, cooled, dissolved in dilute nitric acid, and precipitated with silver nitrate. Any silver chloride is collected and weighed and calculated into chloroform.*

VI.—OTHER ANÆSTHETICS.

When chlorine acts upon marsh-gas, the hydrogen can be displaced atom by atom ; and from the original methane (CH_4) can be successively obtained chloromethane or methyl chloride (CH_3Cl), dichloromethane, or methene dichloride, methylene dichloride, (CH_2Cl_2), trichloromethane or chloroform, (CHCl_3), already described, and carbon tetrachloride (CCl_4). All these are, more or less, capable of producing anaesthesia ; but none of them, save chloroform, are of any toxicological importance.

Methene dichloride, recommended by Dr. W. B. Richardson as an anaesthetic, has come somewhat into use. It is a colourless, very volatile liquid, of specific gravity 1.360, and boiling at 41°. It burns with a smoky flame, and dissolves iodine with a brown colour.

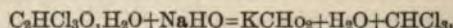
Paraldehyde ($\text{C}_6\text{H}_{12}\text{O}_3$) is a colourless fluid, boiling at 124° ; specific gravity .998 at 15°. By the action of cold it may be obtained in crystals, the melting point of which is 10.5°. It is soluble in eight parts of water at 13°, in warm water it is less soluble ; hence, on warming a solution, it becomes turbid. Paraldehyde acts very similar to chloral ; it causes a deep sleep, and (judging by experiments on animals) produces no convulsive movements. Possibly it is less dangerous than chloral, and might supplant the latter as a remedy. (See a paper in the *Archiv für Exper. Pathol. u. Pharmakol.*, Leips., 1882).

* S. Vidali has made the ingenious suggestion of developing hydrogen in the usual way, by means of zinc and sulphuric acid, in the liquid supposed to contain chloroform, to ignite the hydrogen, as in Marsh's test, when it issues from the tube, and then to hold in the flame a clean copper wire. Since any chloroform is burnt up in the hydrogen flame to hydrochloric acid, the chloride of copper immediately volatilises and colours the flame green.

VII.—CHLORAL.

Chloral Hydrate ($C_2H_3Cl_3O_2$) is made by mixing equivalent quantities of anhydrous chloral * and water. The purest chloral is in the form of small, granular, sugar-like crystals; when less pure, the crystals are larger. These melt into a clear fluid at from 48° to 49° , and the melted mass solidifies again at a little below 50° . Chloral boils at 97.5° ; it is not very soluble in cold chloroform, requiring four times its weight. The only substance with which chloral hydrate may well be confused is chloral alcoholate ($C_4H_7Cl_3O_2$) but chloral alcoholate melts at a lower temperature (45°), and boils at a higher (113.5°); it is easily soluble in cold chloroform, and inflames readily, whereas chloral scarcely burns.

Chloral hydrate completely volatilises, and can be distilled in a vacuum without change. If, however, boiled in air, it undergoes slow decomposition, the first portions of the distillate being overhydrated, the last underhydrated; the boiling point, therefore, undergoes a continuous rise. The amount of hydration of a commercial sample is of practical importance; if too much water is present, the chloral deliquesces, especially in warm weather; if too little, it may become acid, and in part insoluble from the formation of meta-chloral ($C_6H_3Cl_3O_3$). Chloral hydrate, by the action of the volatile or fixed alkalies, is decomposed, an alkaline formate and chloroform resulting thus—



Trichlor-acetic acid is decomposed in a similar manner.

It is, of course, obvious that after splitting up chloral into chloroform, the latter can be detected by distillation and applying the tests given at p. 131 and *seq.* Chloral hydrate is soluble in one and a half times its weight of water; the solution should be perfectly neutral to litmus. It is also soluble in ether, in alcohol, and in carbon disulphide. There should be no cloudiness when a solution is tested with silver nitrate in the cold; if, however, to a boiling solution nitrate of silver and a little ammonia are added, there is a mirror of reduced silver.

The assay of chloral hydrate in solution is best effected by distilling the solution with slaked lime, the distillate is received in water contained in a graduated tube, kept at a low temperature. The chloroform sinks to the bottom and is directly read off; the number of cc. multiplied by 2.64 equals the weight of the chloral hydrate present.

* Anhydrous chloral (C_2HCl_3O), is an oily liquid, of specific gravity 1.502 at 18° ; it boils at 94° . It is obtained by the prolonged action of chlorine on absolute alcohol.

Another method, accurate but only applicable to the fairly pure substance, is to dissolve 1 to 2 grms. in water, remove any free acid by baric carbonate, and then treat the liquid thus purified by a known volume of standard soda. The soda is now titrated back, using litmus as an indicator, each cc. of normal alkali utralised by the sample corresponds to 1.655 grms. of chloral hydrate. Small quantities of chloral hydrate may be conveniently recovered from complex liquids by shaking them up with ether, and removing the ethereal layer, in the tube represented in Fig. 10. The ether must be allowed to evaporate spontaneously ; but there is in this way much loss of chloral. The best method of estimating minute quantities is to alkalise the liquid, and slowly distil the vapour through a red-hot combustion-tube charged with pure lime, as in the process described at p. 132.

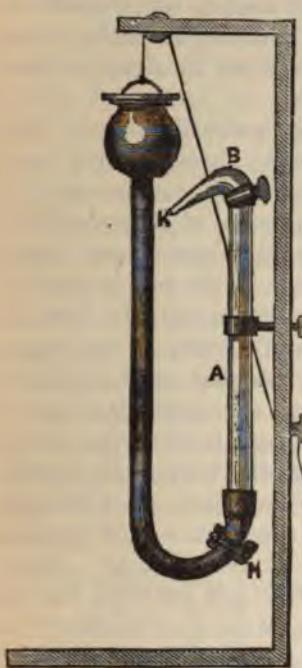


Fig. 10.*

paralysing the automatic centre. The heart, as in animals, poisoned by atropine, stops in diastole, and the blood-pressure sinks in proportion to

* The figure is from vol. i., "Foods," p. 69, the description may be here repeated :—“A is a tube of any dimensions most convenient to the analyst. Ordinary burette size will perhaps be the most suitable for routine work ; the tube is furnished with a stopcock and is bent at B, the tube at K having a very small but not quite capillary bore. The lower end is attached to a length of pressure-tubing, and is connected with a small reservoir of mercury, moving up and down by means of a pulley. To use the apparatus : Fill the tube with mercury by opening the clamp at H, and the stopcock at B, and raising the reservoir until the mercury, if allowed, would flow out of the beak. Now, the beak is dipped into the liquid to be extracted with the solvent, and by lowering the reservoir, a strong vacuum is created, which draws the liquid into the tube ; in the same way the ether is made to follow. Should the liquid be so thick that it is not possible to get it in by means of suction, the lower end of the tube is disconnected, and the syrupy mass worked in through the wide end. When the ether has been sucked into the apparatus, it is emptied of mercury by lowering the reservoir, and then firmly clamped at H, and the stopcock also closed. The tube may now be shaken, and then allowed to stand for the liquids to separate. When

Effects of Chloral Hydrate on Animals.

—Experiments on animals have taught us all that is known of the physiological action of chloral. It has been shown that the drug influences very considerably the circulation, at first exciting the heart's action, and then

the progressive paralysis of the cardiac centre. At the same time, the respiration is slowed and finally ceases, while the heart continues to beat. The body temperature of the warm-blooded animals is very remarkably depressed, according to Falck, even to 7.6° . Vomiting has been rather frequently observed with dogs and cats, even when the drug has been taken into the system by subcutaneous injection.

The secretion of milk, according to Röhrgig, is also diminished. Reflex actions through small doses are intensified; through large, much diminished. '025-'05 grm. (4-'7 grain), injected subcutaneously into frogs causes a slowing of the respiration, a diminution of reflex excitability, and lastly, its complete cessation; this condition lasts several hours; at length the animal returns to its normal state. If the dose is raised to '1 grm. (1.5 grain) after the cessation of reflex movements, the heart is paralysed—and a paralysis not due to any central action of the vagus, but to a direct action on the cardiac ganglia. Rabbits of the ordinary weight of 2 kilos. are fully narcotised by the subcutaneous injection of 1 grm.; the sleep is very profound, and lasts several hours; the animal wakes up spontaneously, and is apparently none the worse. If 2 grms. are administered, the narcotic effects, rapidly developed, are much prolonged. There is a remarkable diminution of temperature, and the animal dies, the respiration ceasing without convulsion or other sign. Moderate-sized dogs require 6 grms. for a full narcosis, and the symptoms are similar; they also wake after many hours, in apparent good health.*

Liebreich considered that the action of chloral was due to its being broken up by the alkali of the blood, and the system being thus brought into a state precisely similar to its condition when anaesthetised by chloroform-vapour. This view has, however, been proved to be erroneous. Chloral hydrate can, it is true, be decomposed in some degree by the blood at 40° ; but the action must be prolonged for several hours. A 1 per cent. solution of alkali does not decompose chloral at a blood-heat in the time within which chloral acts in the body; and since narcotic effects are commonly observed when, in the fatty group, hydrogen has been displaced by chlorine, it is more probable that chloral hydrate is absorbed and circulates in the blood as such, and is not broken up into chloroform and an alkaline formiate.

there is a good line of demarcation, by raising the reservoir after opening the clamp and stopcock, the whole of the light solvent can be run out of the tube into a flask or beaker, and recovered by distillation. For heavy solvents (such as chloroform), which sink to the bottom, a simple burette with a fine exit tube is preferable; but for petroleum ether, ordinary ether, &c., the apparatus figured is extremely useful.

* C. Ph. Falck has divided the symptoms into (1) Preliminary hypnotic; (2) an adynamic state; and (3) a comatose condition.

Effects of Chloral Hydrate on Man.—Since the year 1869, in which chloral was first introduced to medicine, it has been the cause of a number of accidental and other cases of poisoning. I find, up to the present time, recorded in medical literature, thirty-one cases of poisoning by chloral hydrate. This number is a small proportion only of the actual number dying from this cause. In nearly all the cases, the poison was taken by the mouth, but in one instance the patient died in three hours, after having injected into the rectum 5·86 grms. of chloral hydrate. There is also on record a case in which, for the purpose of producing surgical anaesthesia, 6 grms. of chloral were injected into the veins; the man died in as many minutes.*

Fatal Dose.—It is impossible to state with any exactness the precise quantity of chloral which may cause death. Children bear it better, in proportion, than adults, while old persons, (especially those with weak hearts, and those inclined to apoplexy) are likely to be strongly affected by very small doses. A dose of 1·9 grm. (3 grains) has been fatal to a child a year old in ten hours. On the other hand, according to Bouchut's observations on 10,000 children, he considers that the full therapeutic effect of chloral can be obtained safely with them in the following ratio :—

Children of 1 to 3 years, dose	1 to 1·5 grm.	(15·4 to 23·1 grain.)
" 3 " 5 "	2 " 3 "	(30·8 " 46·3 ")
" 5 " 7 "	3 " 4 "	(46·3 " 61·7 ")

These quantities being dissolved in 100 cc. of water.

These doses are certainly too high, and it would be dangerous to take them as a guide, since death has occurred in a child, aged five, from a dose of 3 grm. (46·3 grains). Medical men in England consider 20 grains a very full dose for a child of four years old, and 50 for an adult, while a case is recorded in which a dose of 1·9 grm. (30 grains) proved fatal in thirty-five hours to a young lady aged twenty. On the

* This dangerous practice was introduced by M. Ore. In a case of traumatic tetanus, in which M. Ore injected into the veins 9 grms. of chloral in 10 grms. of water, there was profound insensibility lasting eleven hours, during which time a painful operation on the thumb was performed. The next day 10 grms. were injected, when the insensibility lasted eight hours; and 9 grms. were injected on each of the two following days. The man recovered. In another case, Ore anaesthetised immediately a patient by plunging the subcutaneous needle of his syringe into the radial vein, and injected 10 grms. of chloral hydrate with 30 of water. The patient became insensible before the whole quantity was injected with "une immobilité rappelant celle du cadavre." On finishing the operation, the patient was roused by the application of an electric current, one pole on the left side of the neck, the other on the epigastrium.—*Journ. de Pharm. et de Chimie.* t. 19, p. 314.

other hand, we find a case * in which, to a patient suffering from epileptic mania, a dose of 31·1 grms. (1 oz) of chloral hydrate was administered; she sank into a deep sleep in five minutes. Subcutaneous injections of strychnine were applied, and after sleeping for forty-eight hours, there was recovery. On the third day a vivid scarlatinal rash appeared, followed by desquamation. The examples quoted—the fatal dose of 1·9 grm., and recovery from 31 grms.—are the two extremes for adults. From other cases, it appears tolerably plain that most people would recover, especially with appropriate treatment, from a single dose under 8 grms., but anything above that quantity taken at one time would be very dangerous, and doses of 10 grms. and above, almost always fatal. If, however, 8 grms. were taken in divided doses during the twenty-four hours, it could (according to Dr. Richardson) be done with safety. The time from the taking of the poison till death varies considerably, and is in part dependent on the dose.

In seven cases of lethal poisoning, three persons who took the small doses of 1·25, 2·5, and 1·95 grm. respectively, lived from eight to ten hours; two taking 4 and 5 grms. respectively, died very shortly after the administration of the chloral. In a sixth case, related by Brown, in which 3·12 grms. had been taken, the patient lived an hour; and in another, after a dose of 5 grms., recorded by Jolly, death took place within a quarter of an hour.

Symptoms.—With moderate doses there are practically no symptoms, save a drowsiness coming on imperceptibly and followed by heavy sleep. With doses up to 2 grms. (30·8 grains), the hypnotic state is perfectly under the command of the will, and if the person chooses to walk about or engage in any occupation, he can ward off sleep; but with those doses which lead to danger, the narcosis is completely uncontrollable; the appearance of the sleeper is often strikingly like that of a drunken person. There is great diminution of temperature commencing in from five to twenty minutes after taking the dose—occasionally sleep is preceded by a delirious state. During the deep slumber the face is much flushed, and in a few cases the sleep passes directly into death without any marked change. In others, symptoms of collapse appear, and the patient sinks through exhaustion.

With some persons doses, which, in themselves, are insufficient to cause death, yet have a peculiar effect on the mental faculties. A case of great medico-legal interest is described by the patient himself, Dr. Manjot†. He took in three doses, hourly, 12 grms. of chloral hydrate. After the first dose the pain, for which he had recourse to chloral, van-

* *Chicago Medical Review*, 1882.

† *Gaz. des Hop.*, 1875.

ished, but, Manjot, although he had all the appearance of being perfectly conscious, yet had not the slightest knowledge of what he was doing or speaking. He took the other two doses, and sank into a deep sleep which lasted twelve hours. He then awoke and answered questions with difficulty, but could not move ; he lay for the next twelve hours in a half-sleep, and the following night slept soundly—to wake up recovered.

The treatment of acute chloral poisoning which has been most successful is that by strychnine injections, and the application of warmth to counteract the loss of temperature which is so constant a phenomenon. As an illustration of the treatment by strychnine, an interesting case recorded by Levinstein* may be quoted.

A man, thirty-five years old, took at one dose, for the purpose of suicide, 24 grms. of chloral hydrate. In half a hour afterwards he was found in a deep sleep, with flushed face, swollen veins, and a pulse 160 in the minute. After a further half-hour, the congestion of the head was still more striking ; the temperature was 39.5° ; the pulse hard and bounding 92 ; the breathing laboured, at times intermittent.

Artificial respiration was at once commenced, but in spite of this, in about another half-hour, the face became deadly pale, the temperature sank to 32.9°. The pupils contracted, and the pulse was scarcely to be felt ; 3 mgrms. (.04 grain) of strychnine were now injected subcutaneously ; this caused tetanic convulsions in the upper part of the body and trismus. The heart's action again became somewhat stronger, the temperature rose to 33.3°, and the pupils dilated ; but soon followed, again, depression of the heart's action, and the respiration could only be kept going by faradisation. Two mgrms. (.03 grain) of strychnine were once more injected, and the heart's action improved. During the succeeding six hours the respiration had to be assisted by faradisation. The temperature gradually rose to 36.5° ; ten hours after taking the dose the patient lay in a deep sleep, breathing spontaneously and reacting to external stimuli with a temperature of 38.5°. Eighteen hours from the commencement, the respiration again became irregular and the galvanic current was anew applied. The last application aroused the sleeper ; he took some milk and again slept ; after twenty-seven hours he could be awakened by calling, &c., but had not full consciousness ; he again took some milk and sank to sleep. It was not until thirty-two hours had elapsed from the ingestion of the poison that he awoke spontaneously ; there were no after effects.

Chronic Poisoning by Chloral Hydrate.—An enormous number of people take habitually chloral hydrate. The history of the habit is

* *Vierteljahrsschr. f. Ger. Med.*, Bd. xx, 1874.

usually that some physician has given them a chloral prescription for neuralgia, for loss of sleep, or other cause, and finding that they can conjure sleep, oblivion and loss (it may be) of suffering whenever they choose, they go on repeating it from day to day until it becomes a necessity of their existence. A dangerous facility to chloral-drinking is the existence of patent medicines, advertised as sleep-producers, and containing chloral as the active ingredient. A lady aged thirty-five died in 1876, at Exeter, from an overdose of "Hunter's solution of chloral, or sedative draught and sleep producer." Its strength was stated at the inquest to be 25 grains to the drachm (1·6 per cent.)*

The evil results of this chloral drinking are especially to be looked for in the mental faculties, and the alienists have had since 1869 a new insanity-producing factor. In a visit made a little time ago to some of the leading asylums, I found several cases of melancholia and mania referred rightly (or wrongly) to chloral-drinking. Symptoms other than those of the brain are chilliness of the body, inclination to fainting, clonic convulsions, and a want of coördination of the muscles of the lower extremities. In a case recorded by Husband,† a lady, after twelve days treatment by chloral hydrate, in doses of from 1 to 2 grms. (15·4 to 30·8 grains), suffered from a scarlatina-like rash, which was followed by desquamation (see also *ante*, p. 138). Among the insane, it has also been noticed that its use has been followed by nettle-rash and petechiae (Reimer and others).

The exact manner in which chloral leaves the body is not sufficiently worked out; a small part is excreted undecomposed, and, according to Musculus and Mering,‡ a part is excreted in the form of uro-chloral acid. This acid occurs in colourless groups of needles similar to tyrosin. They are soluble in alcohol, in ether-alcohol, and in water, but insoluble in ether. They turn a ray of polarised light to the left, reduce silver solutions on boiling, and colour yellow an indigo solution alkaliised by soda. They do not respond to the aniline and soda test (p. 132).

Separation of Chloral from Organic Matters.—It will be most convenient to place the organic fluid or pulped-up solid, mixed with water, in a retort, to acidify with tartaric or phosphoric acid, and to distil; in this way, the expert will not confuse chloral with chloroform, for any chloroform will pass over, and can be identified by the tests given at p. 132, and the chloral hydrate, if present, will remain undecomposed. On now making the contents of the retort strongly alkaline, the chloral is decomposed, and any chloroform derived from it will distil. If traces

* *Exeter and Plymouth Gazette*, Jan. 12, 1876.

† *Lancet*, 1871.

‡ *Ber. d. Chem. Ges.*, 8 Band.

only are likely to be present (as in operating on the blood or urine), then the distillate should not be condensed, but dealt with as recommended at p. 132. I have nothing of value to add with regard to the tests already enumerated, save that Dr. Frank Ogston* has recommended sulphide of ammonium to be added to any liquid as a test for chloral. The contents of the stomach are filtered or submitted to dialysis, and the test applied direct. If chloral is present, there is first an orange-yellow colour; on standing, the fluid becomes more and more brown, then troubled, an amorphous precipitate falls to the bottom, and a peculiar odour is developed. With 10 mgrms. of chloral in 1 cc. of water, there is an evident precipitate, and the odour can readily be perceived; with 1 mgrm. dissolved in 1 cc. of water, there is an orange-yellow colour, and also the odour, but no precipitate; with 1 mgrm. in 1 cc. of water, there is a weak, pale, straw-yellow colour, which can scarcely be called characteristic. The only substance giving in neutral solutions the same reactions is antimony; but on the addition of a few drops of acid, the antimony falls as an orange-yellow precipitate, while, if chloral alone is present, there is a light white precipitate of sulphur.

VIII.—BISULPHIDE OF CARBON.

Bisulphide of carbon—carbon disulphide, carbon sulphide (CS₂)—is a colourless, volatile fluid, strongly refracting light. Commercial samples have a most repulsive and penetrating odour, but chemically-pure carbon sulphide has a smell which is not disagreeable. The boiling point is 47°; the specific gravity at 0° is 1.293. It is very inflammable, burning with a blue flame, and evolving sulphur dioxide; is little soluble in water, but mixes easily with alcohol or ether. Bisulphide of carbon, on account of its solvent powers of sulphur, phosphorus oils, resins, caoutchouc, gutta-purcha, &c., is in great request in certain industries. It is also utilised for disinfecting purposes, the liquid being burnt in a lamp.

Poisoning by Carbon Bisulphide.—In spite of the cheapness and numerous applications of this liquid, poisoning is very rare. There appears to be a case on record of attempted self-destruction by this agent, in which a man took 2 ounces (56.7 cc.) of the liquid, but without a fatal result. The symptoms in this case were pallor of the face, wide pupils, frequent and weak pulse, lessened bodily temperature, and spasmodic convulsions. Carbon disulphide was detected in the breath by leading the expired air through an alcoholic solution of try-ethylphos-

* *Vierteljahrsschrift f. Gerichtl. Medicin*, 1879, Bd. xxx., Hft. 1, S. 268.

phin, with which it struck a red colour. It could also be found in the urine in the same way. An intense burning in the throat, giddiness, and headache lasted for several days. Experiments on animals have been frequent, and it is found to be fatal to all forms of animal life. There is, indeed, no more convenient agent for the destruction of various noxious insects, such as moths, the weevils in biscuits, the common bug, &c., than bisulphide of carbon. It has also been recommended for use in exterminating mice and rats.*

Different animals show varying degrees of sensitiveness to the vapour; frogs and cats being less affected by it than birds, rabbits, and guinea-pigs. The action on animals seems to have great similarity to that of chloroform. There is complete anaesthesia of the whole body, and death occurs through paralysis of the respiratory centre, but artificial respiration fails to restore life.

Chronic Poisoning.—Of some importance is the chronic poisoning by carbon disulphide, occasionally met with in manufactures necessitating the daily use of large quantities for dissolving caoutchouc, &c. When taken thus in the form of vapour daily for some time, it gives rise to a complex series of symptoms which may be divided into two principal stages—viz., a stage of excitement, and one of depression. In the first phase, there is a more or less permanent headache, with considerable indigestion, and its attendant loss of appetite, nausea, &c. The sensitiveness of the skin is also heightened, and there are curious sensations of creeping, &c. The mind at the same time in some degree suffers, the temper becomes irritable, and singing in the ears and noises in the head have been noticed. In one factory a workman suffered from an acute mania, which subsided in two days upon removing him from the noxious vapour (Eulenberg). The sleep is disturbed by dreams, and, according to Delpech,† there is considerable sexual excitement, but this statement has been in no way confirmed. Pains in the limbs are a constant phenomenon, and the French observers have noticed spasmodic contractions of certain groups of muscles.

The stage of depression begins with a more or less pronounced anaesthesia of the skin. This is not confined to the outer skin, but also affects the mucous membranes; patients complain that they feel as if the tongue were covered with a cloth. The anaesthesia is very general. In a case recorded by Bernhardt,‡ a girl, twenty-two years old, who had worked six weeks in a caoutchouc factory, suffered from mental weakness and digestive troubles; there was anaesthesia and algesia of the whole

* Cloëz, *Compt. Rend.*, 63 Bd. 85.

† *Mémoire sur les Accidents que developpe chez les ouvrières en caoutchouc du sulfure de carb. en vapeur.* Paris, 1865.

‡ *Ber. Klin. Wochenschrift*, No. 32, 1866.

skin. In these advanced cases the mental debility is very pronounced, and there is also weakness of the muscular system. Paralysis of the lower limbs has been noted, and in one instance a man had his right hand paralysed for two months. It seems uncertain how long a person is likely to suffer from the effects of the vapour after he is removed from its influence. If the first stage of poisoning only is experienced, then recovery is generally rapid; but if mental and muscular weakness and anaesthesia of the skin have been developed, a year has been known to elapse without any considerable improvement, and permanent injury to the health may be feared.

Post-mortem Appearances.—The pathological appearances found after sudden death from disulphide of carbon are but little different to those found after fatal chloroform breathing.

Detection and Separation of Carbon Disulphide.—The extreme volatility of the liquid renders it easy to separate it from organic liquids by distillation. If it is necessary to make a quantitative estimation, then the organic or other liquid must be distilled with all the precautions described at page 123 when speaking of ether. Carbon disulphide is identified (1) by its odour; (2) by its boiling point; (3) by its action on an alcoholic solution of potash, potassic xanthogenate ($CS_2C_2H_5OK$) being formed, which gives a yellow precipitate with cupric sulphate; (4) heated with lead nitrate and potash, a black precipitate of lead sulphide is obtained.

Xanthogenic acid or ethyloxide-sulphocarbonate ($CS_2C_2H_5OH$) is prepared by decomposing potassic xanthogenate by diluted hydrochloric or sulphuric acid. It is a colourless fluid, having an unpleasant odour, and a weakly acid, and rather bitter taste. It burns with a blue colour, and is easily decomposed at 24° , splitting up into ethylic alcohol and hydric sulphide. It is very poisonous, and has an anaesthetic action similar to bisulphide of carbon.

Potassic xanthogenate ($CS_2C_2H_5OK$) and *potassic xanthamylate* ($CS_2C_2H_1OK$) (the latter being prepared by the substitution of amyl alcohol for ethyl alcohol) both on the application of a heat below that of the body, develop CS_2 , and are poisonous, inducing symptoms very similar to those already detailed.

IX.—CARBOLIC ACID.

Carbolic Acid. Syn. Phenol, Phenyl Alcohol, Phenylc Hydrate; Phenic Acid; Coal Tar Creasote.—The formula for carbolic acid is C_6H_5HO . The pure substance appears at the ordinary temperature as a colourless solid, crystallising in long prisms; the fusibility of the crystals is given variously by different authors; from my own observation, I be-

lieve the pure crystals to melt at about 42° , any lower melting-point being due to the presence of cresylic acid or other impurity; the crystals again become solid about 15° . Melted carbolic acid forms a colourless limpid fluid, sinking in water. It boils under the ordinary pressure at 182° , and distils without decomposition; it is very readily and completely distilled in a vacuum at about the temperature of 100° . After the crystals have been exposed to the air, they absorb water, and a hydrate is formed containing 16.07 per cent. of water. The hydrate melts at 17° , any greater hydration prevents the crystallisation of the acid; a carbolic acid, containing about 27 per cent. of water, and probably corresponding to the formula $C_6H_6O \cdot 2H_2O$, is obtained by gradually adding water to carbolic acid so long as it continues to be dissolved. Such a hydrate dissolves in 11.1 times its measure of water, and contains 8.56 per cent. of real carbolic acid. Carbolic acid does not redden litmus, but produces a greasy stain on paper, disappearing on exposure to the air; it has a peculiar smell, a burning, numbing taste, and in the fluid state it strongly refracts light. Heated to a high temperature it takes fire, and burns with a sooty flame.

When an aqueous solution of carbolic acid is shaken up with ether, benzene, carbon disulphide, or chloroform, it is fully dissolved by the solvent, and is thus easily separated from most solutions in which it exists in the free state. Petroleum ether, on the other hand, only slightly dissolves it in the cold, more on warming. Carbolic acid mixes in all proportions with glycerine, glacial or acetic acid, and alcohol. It coagulates albumen, the precipitate being soluble in an excess of albumen; it also dissolves iodine, without changing its properties. It dissolves many resins, and also sulphur, but, on boiling, sulphuretted hydrogen is disengaged. Indigo blue is soluble in hot carbolic acid, and may be obtained in crystals on cooling. Carbolic acid is contained in castoreum, a secretion derived from the beaver, but it has not yet been detected in the vegetable kingdom. The source of carbolic acid is at present coal-tar, from which it is obtained by a process of distillation. There are, however, a variety of chemical actions in the course of which carbolic acid is formed.

The common disinfecting carbolic acid is a dark-reddish liquid, with a very strong odour, containing carbolic acid, cresylic acid, and other phenols. It is officinal in Germany, and there must contain at least 50 per cent. of the pure carbolic acid. The pure crystallised acid is officinal in our own and all the continental pharmacopœias. In the British Pharmacopœia, a solution of carbolic acid in glycerine is officinal; the proportions are one part of carbolic acid and four parts of glycerine, that is, strength 20 per cent. The Pharmacopœia Germanica has a *liquor natri carbolicici*, made with five parts carbolic acid, one caustic soda, and four of water; strength in carbolic acid—50 per cent. There is also a strongly alkaline crude sodic carbolate in use as a preservative of wood.

There are various disinfecting fluids containing various amounts of carbolic acid, from 10 per cent. upwards. Many of these are somewhat complex mixtures, but, as a rule, any poisonous properties they possess are mainly due to their content of carbolic acid. A great variety of disinfecting powders, under various names, are also in commerce, deriving their activity from carbolic acid. Macdougall's disinfecting powder is made by adding a certain proportion of impure carbolic acid to a calcic sulphite, which is prepared by passing sulphur dioxide over ignited limestone.

Calvert's carbolic acid powder is made by adding carbolic acid to the siliceous residue obtained from the manufacture of aluminic sulphate from shale. There are also various carbolates which, by heating or decomposing with sulphuric acid, give off carbolic acid.

Carbolic acid soaps are also made on a large scale—the acid is free, and some of the soaps contain as much as ten per cent. In the inferior carbolic acid soaps there is little or no carbolic acid, but cresylic takes its place. Neither the soaps nor the powders have hitherto attained any toxicological importance, but the alkaline carbolates are very poisonous.

The chief uses of carbolic acid are indicated by the foregoing enumeration of the principal preparations used in medicine and commerce. The bulk of the carbolic acid manufactured is for the purposes of disinfection. It is also utilised in the preparation of certain colouring matters or dyes, and during the last few years has had another application in the manufacture of salicylic acid. In medicine it is administered occasionally internally, while the antiseptic movement in surgery, initiated by Lister, has given it great prominence in surgical operations.

Statistics.—Carbolic acid is, of all powerful poisons, the most accessible, and the most recklessly distributed. We find it at the bedside of the sick, in back-kitchens, in stables, in public and private closets and urinals, and, indeed, in almost all places where there are likely to be foul odours or decomposing matters. It is, therefore, no wonder that poisoning by carbolic acid has, of late years, assumed large proportions. The acid has become vulgarised, and quite as popularly known, as the most common household drugs or chemicals.* This familiarity is the growth of a very few years, since it was not discovered until 1834, and does not seem to have been used by Lister until about 1863. It was not known to the people generally until much later. At present it occupies the sixth place in fatality of all poisons in England.

* Although this is so, yet much ignorance still prevails as to its real nature. In a case reported in the *Pharm. Journal*, 1881, p. 334, a woman, thirty years of age, drank two-thirds of an ounce of liquid labelled "Pure Carbolic Acid" by mistake, and died in two hours. She read the label, and a lodger also read it, but did not know what it meant.

Falck has collected, since the year 1868, no less than eighty-seven cases of poisoning from carbolic acid recorded in medical literature. In one of the cases the individual died in nine hours from a large dose of carbolate of soda ; in a second, violent symptoms were induced by breathing for three hours carbolic acid vapour ; in the remaining eighty-five, the poisoning was caused by the liquid acid. Of these eighty-five persons, seven had taken the poison with suicidal intent, and of the seven, five died ; thirty-nine were poisoned through the medicinal use of carbolic acid, twenty-seven of the thirty-nine by the antiseptic treatment of wounds by carbolic acid dressings, and of these eight terminated fatally ; in eight cases symptoms of poisoning followed the rubbing or painting of the acid on the skin for the cure of scabies, favus, or psoriasis, and six of these patients died. In four cases, carbolic acid enemata, administered for the purpose of dislodging ascarides, gave rise to symptoms of poisoning, and, in one instance, death followed.

The substitution of carbolic acid for medicine happened as follows :—

	Cases.
Taken instead of Tincture of Opium,	1
“ “ Infusion of Senna,	3
“ “ Mineral Water,	2
“ “ other Mixtures,	3
“ inward instead of outward application,	3
	—
	12

Of these twelve, eight died.

Again, ten persons took carbolic acid in mistake for various alcoholic drinks, such as Schnapps, brandy, rum, or beer, and nine of the ten succumbed ; seventeen persons drank carbolic acid simply “ by mistake,” and of these, thirteen died. Thus, of the whole eighty-five cases, no less than fifty-one ended fatally,—nearly 60 per cent.

Fatal Dose.—The minimum fatal dose for cats, dogs, and rabbits, appears to be from ‘4 to ‘5 grm. per kilogram. Falck has put the minimum lethal dose for man at 15 grms. (231.5 grains), which would be about ‘2 per kilo., basing his estimate on the following reasoning. In thirty-three cases he had a fairly exact record of the amount of acid taken, and, out of the thirty-three, he selects only those cases which are of use for the decision of the question. Among adults in five cases the dose was 30 grms., and all the five cases terminated by death, in times varying from five minutes to an hour and a half. By other five adults a dose of 15 grms. was taken ; of the five, three men and one woman died in times varying from forty-five minutes to thirty hours, while one woman recovered. Doses of 11.5, 10.8, and 9 grms. were taken by different men, and recovered from ; on the other hand, a suicide who took one

and a half teaspoonful (about 6 grms.) of the concentrated acid, died in fifty minutes. Doses of '3 to 3 grms have caused symptoms of poisoning, but the patients recovered, while higher doses than 15 grms. in twelve cases, with only one exception, caused death. Hence, it may be considered tolerably well established, that 15 grms. (231.5 grains) may be taken as representing the minimum lethal dose.

The largest dose from which a person appears to have recovered is, I believe, that given in a case recorded by Davidson in which 150 grms. of crude carbolic acid had been taken. It must, however, be remembered that as this was the impure acid, probably only half of it was really carbolic acid. The German Pharmacopeia prescribes as a maximum dose '05 (.7 grain) of the crystallised acid, and a daily maximum quantity given in divided doses of '15 grm. (2.3 grains).

Effects on Animals.—Carbolic acid is poisonous to both animal and vegetable life.

Infusoria.—One part of the acid in 10,000 parts of water rapidly kills ciliated animalcules,—the movements become sluggish, the sarcode substance darker, and the cilia in a little time cease moving.

Fish.—One part of the acid in 7,000 of water kills dace, minnows, roach, and gold fish. In this amount of dilution the effect is not apparent immediately ; but, at the end of a few hours, the movements of the fish become sluggish, they frequently rise to the surface to breathe, and at the end of twenty-four hours are found dead. Quantities of carbolic acid, such as one part in 100,000 of water, appear to affect the health of fish, and render them more liable to be attacked by the fungus growth which is so destructive to fish-life in certain years.

Frogs.—If '01 to '02 grm. of carbolic acid be dissolved in a litre of water in which a frog is placed, there is almost immediately signs of uneasiness in the animal, showing that pain from local contact is experienced ; a sleepy condition follows, with exaltation of reflex sensibility ; convulsions succeed, generally, though not always ; then reflex sensibility is diminished, ultimately vanishes, and death occurs ; the muscles and nerves still respond to the electric current, and the heart beats, but slowly and weakly, for a little after the respiration has ceased.

Warm-blooded Animals.—For a rabbit of the average weight of 2 kilo., '15 grm. is an active dose and '3 a lethal dose (that is '15 per kilo). The sleepy condition of the frog is not noticed, and the chief symptoms are clonic convulsions with dilatation of the pupils, the convulsions passing into death, without a noticeable paralytic stage. The symptoms observed in poisoned dogs are almost precisely similar, the dose according to body-weight being the same. It has, however, been noticed that with doses large enough to produce convulsions, a weak condition has supervened, causing death in several days. There appears to be no cumulative

action, since equal toxic doses can be given to animals for some time, and the last dose has no greater effect than the first or intermediate ones. The pathological appearances met with in animals poisoned by the minimum lethal doses referred to are not characteristic; but there is a remarkable retardation of putrefaction.

Symptoms in Man, External Application.—A 5 per cent. solution of carbolic acid, applied to the skin, causes a peculiar numbness, followed, it may be, by irritation. Young subjects, and those with sensitive skins, sometimes exhibit a pustular eruption, and concentrated solutions cause more or less destruction of the skin. Lemaire* describes the action of carbolic acid on the skin as causing a slight inflammation, with desquamation of the epithelium, followed by a very prominent brown stain, but this he alone has observed. Applied to the mucous membrane, carbolic acid turns the epithelial covering white; the epithelium, however, is soon thrown off, and the place rapidly heals; there is the same numbing, aconite-like feeling before noticed. The vapour of carbolic acid causes redness of the conjunctiva, and irritation of the air-passages. If the application is continued, the mucous membrane swells, whitens, and pours out an abundant secretion.

Dr. Whitelock of Greenock has related two instances in which children were treated with carbolic acid lotion (strength $2\frac{1}{2}$ per cent.) as an application to the scalp for ringworm; in both, symptoms of poisoning occurred—in the one, the symptoms at once appeared; in the other, they were delayed for some days. In order to satisfy his mind, the experiment was repeated twice, and each time gastric and urinary troubles followed.

Nussbaum of Munich records a case† in which symptoms were induced by the forcible injection of a solution of carbolic acid into the cavity of an abscess.

Macphail‡ gives two cases of poisoning by carbolic acid from external use. In the one, a large tumor had been removed from a woman aged thirty, and the wound covered with gauze steeped in a solution of carbolic acid, in glycerine, strength 10 per cent.; subsequently there was high fever, with diminished sulphates in the urine, which smelt strongly of carbolic acid, and was very dark. On substituting boracic acid, none of these troubles were observed. The second case was that of a servant suffering from axillary abscess; the wound was syringed out with carbolic acid solution, of strength $2\frac{1}{2}$ per cent., when effects were produced

* Lemaire, Jul., "De l'Acide phenique." Paris, 1864.

† *Leitfaden zur Antiseptischer Wundbehandlung*, 141.

‡ "Carbolic Acid Poisoning (Surgical)," by S. Rutherford Macphail, M.B., *Ed. Med. Journal*, ccxiv., Aug., 1881, p. 134.

similar to those in the first case. It was noted that in both these cases the pulse was slowed. Scattered throughout surgical and medical literature, there are many other cases recorded, though not all so clear as those cited. Several cases are also on record in which poisonous symptoms (and even death) have resulted from the application of carbolic acid lotion as a remedy for scabies or itch.

A surgeon prescribed for two joiners who suffered from scabies a lotion, which was intended to contain 30 grms. of carbolic acid in 240 cc. of water; but the actual contents of the flasks were afterwards from analysis estimated by Hoppe-Seyler to be 33.26 grms., and the quantity used by each to be equal to 13.37 grms. (206 grains) of carbolic acid. One of the men died; the survivor described his own symptoms as follows:—He and his companion stood in front of the fire, and rubbed the lotion in; he rubbed it into his legs, breast, and the front part of his body; the other parts were mutually rubbed. Whilst rubbing his right arm, and drying it before the fire, he felt a burning sensation, a tightness and giddiness, and mentioned his sensations to his companion, who laughed. This condition lasted from five to seven minutes, but he did not remember whether his companion complained of anything, nor did he know what became of him, nor how he himself came to be in bed. He was found holding on to the joiner's bench, looking with wide staring eyes, like a drunken man, and was delirious for half an hour. The following night he slept uneasily and complained of headache and burning of the skin. The pulse was 68, the appearance of the urine, appetite, and sense of taste were normal; the bowels confined. He soon recovered.

The other joiner seems to have died as suddenly as if he had taken prussic acid. He called to his mother, "Ich habe einen Rausch," and died with pale livid face, after taking two deep, short inspirations.

The *post-mortem* examination showed the sinuses filled with much fluid blood, and the vessels of the pia mater congested. Frothy, dark, fluid blood was found in the lungs, which were hyperæmic; the mucous tissues of the epiglottis and air tubes were reddened, and covered with a frothy slime. Both ventricles—the *venæ cavæ* and the vessels of the spleen and kidneys—were filled with dark fluid blood. The muscles were very red; there was no special odour. Hoppe-Seyler recognised carbolic acid in the blood and different organs of the body.*

In another case, a child died from the outward use of a 2 per cent. solution of carbolic acid. It is described as follows:—An infant of seven weeks old suffered from varicella, and one of the pustules became the centre of an erysipelatous inflammation. To this place a 2 per cent. so-

* R. Köhler, *Würtem. Med. Corr. Bl.*, xlii., No. 6, April, 1872. H. Abelin, *Schmidt's Jahrbücher*, 1877, Bd. 173, S. 163.

lution of carbolic acid was applied by means of a compress steeped in the acid; the following morning the temperature rose from 36.5° (97.7 F.) to 37° (98.6 F.), and poisonous symptoms appeared. The urine was coloured dark. There were sweats, vomitings, and contracted pupils, spasmodyc twitchings of the eyelids and eyes, with strabismus, slow respiration, and lastly, inability to swallow. Under the influence of stimulating remedies the condition temporarily improved, but the child died twenty-three and a half hours after the first application. An examination showed that the vessels of the brain and the tissue of the lungs were abnormally full of blood. The liver was softer than natural, and exhibited a notable yellowishness in the centre of the acini. Somewhat similar appearances were noticed in the kidneys, the microscopic examination of which showed the *tubuli contorti* enlarged and filled with fatty globules. In several places the epithelium was denuded, in other places swollen, and with the nuclei very visible.

In an American case,* death followed the application of carbolic acid to a wound. A boy had been bitten by a dog, and to the wound, at one o'clock in the afternoon, a lotion, consisting of nine parts of carbolic acid and one of glycerine, was applied. At seven o'clock in the evening the child was unconscious, and died at one o'clock the following day.

Internal Administration.—Carbolic acid may be taken into the system, not alone by the mouth, but by the lungs, as in breathing carbolic acid spray or carbolic acid vapour. It is also absorbed by the skin when outwardly applied, or in the dressing or the spraying of wounds with carbolic acid. Lastly, the ordinary poisonous effects have been produced by the absorption from the bowel, when administered as an enema. When swallowed undiluted, and in a concentrated form, the symptoms may be those of early collapse, and speedy death. Hence, the course is very similar to that witnessed in poisoning by the mineral acids.

If lethal, but not excessive, doses of the diluted acid are taken, the symptoms are—a burning in the mouth and throat, a peculiar unpleasant persistent taste, and vomiting. There are faintness and pallor of the face, which is covered by a clammy sweat, and the patient soon becomes unconscious, the pulse small and thready, and the pupils sluggish to light. The respiration is profoundly affected; there is dyspnoea, and the breathing becomes shallow. Death occurs from paralysis of the respiratory apparatus, and the heart is observed to beat for a little after the respiration has ceased. All these symptoms may occur from the application of the acid to the skin or to mucous membranes, and have been noticed when solutions of but moderate strength have been used. There are a series of such cases in gynaecological practice when the

* *American Journal of Pharmacy*, vol. li, 4th Ser.; vol. ix., 1879, p. 57.

mucous membrane (perhaps eroded) of the uterus has been irrigated with carbolic acid injections. Thus, Küster* relates a case in which, four days after confinement, the uterus was washed out with a 2 per cent. solution of carbolic acid without evil results. Afterwards a 5 per cent. solution was used, but it at once caused violent symptoms of poisoning, the face became livid, clonic convulsions came on, and at first loss of consciousness, which after an hour returned. The patient died on the ninth day. There was intense diphtheria of the uterus and vagina. Several other similar cases (although not attended with such marked or fatal effects) are on record.†

The symptoms of carbolic acid poisoning admit of considerable variation from those already described. The condition is occasionally that of deep coma. The convulsions may be general, or may affect only certain groups of muscles.—Convulsive twitchings of the face alone, and also muscular twitchings only of the legs, have been noticed. In all cases, however, a marked change occurs in the urine. Subissi ‡ has noted the occurrence of abortion, both in the pig and the mare, as a result of carbolic acid, but this effect has not hitherto been recorded in the human subject.

It has been experimentally shown by Küster, that previous loss of blood, or the presence of septic fever, renders animals more sensitive to carbolic acid. It is also said that children are more sensitive than adults.

The course of carbolic acid poisoning is very rapid. In 35 cases collected by Falck, in which the period from the taking of the poison to the moment of death was accurately noted, the course was as follows:—12 patients died within the first hour, and in the second hour, 3 ; so that within two hours 15 died. Between the third and the twelfth hour, 10 died ; between the thirteenth and the twenty-fourth hour, 7 died ; and between the twenty-fifth and the sixtieth hour, only 3 died. Therefore, slightly over 71 per cent. died within twelve hours, and 91.4 per cent. within the twenty-four hours.

Changes in the Urine.—The urine of patients who have absorbed in any way carbolic acid is dark in colour, and may smell strongly of the acid. It is now established—chiefly by the experiments and observations

**Central Blatt f. Gynäkologie*, ii., 14, 1878.

† A practitioner in Calcutta injected into the bowel of a boy, aged five, an enema of diluted carbolic acid, which, according to his own statement, was 1 part in 60, and the whole quantity represented 144 grains of the acid. The child became insensible a few minutes after the operation, and died within four hours. There was no *post-mortem* examination ; the body smelt strongly of carbolic acid.—*Lancet*, May 19, 1883.

‡ *L'Archivio della Veterinaria Ital.*, xi., 1874.

of Baumann *—that carbolic acid, when introduced into the body, is mainly eliminated in the form of phenyl-sulphuric acid, $C_6H_5HSO_4$, or more strictly speaking as potassic phenyl-sulphate, $C_6H_5KSO_4$, a substance which is not precipitated by chloride of barium until it has been decomposed by boiling with a mineral acid. Hence it is that, with doses of carbolic acid continually increasing, the amount of sulphates naturally in the urine (as estimated by simply acidifying with hydrochloric acid, and precipitating in the usual way with chloride of barium) continually decreases, and may at last vanish, for all the sulphuric acid present is united with the phenol. On the other hand, the precipitate obtained by boiling, after having first removed the sulphate already deposited by the first operation, is ever increasing.

Thus, a dog voided urine which contained in 100 cc., '262 grm. of precipitable sulphuric acid, and '006 of organically-combined sulphuric acid; his back was now painted with carbolic acid, and the normal proportions were reversed, the precipitable sulphuric acid became '004 grm., while the organically-combined was '190 in 100 cc. In addition to phenyl-sulphuric acid, it is now sufficiently established † that hydroquinone, $(C_6H_4\frac{OH}{OH})$, paradihydroxyl phenol and pyrocatechin, $(C_6H_4\frac{OH}{OH})$ orthodihydroxyl phenol are constant products of a portion of the phenol. The hydroquinone appears in the urine, in the first place, as the corresponding ether-sulphuric acid, which is colourless; but a portion of it is set free, and this free hydroquinone (especially in alkaline urine) is quickly oxidised to a brownish product, and hence the peculiar colour of urine. Out of dark-coloured carbolic acid urine the hydroquinone and its products of decomposition can be obtained by shaking with ether; on separation of the ether, an extract is obtained, reducing alkaline silver solution, and developing quinone on warming with ferric chloride.

To separate pyro-catechin, 200 cc. of urine may be evaporated to an extract, the extract treated with strong alcohol, the alcoholic liquid evaporated, and the extract then treated with ether. On separation and evaporation of the ether a yellowish mass is left, from which the pyrocatechin may be extracted by washing with a small quantity of water. This solution will reduce silver solution in the cold, or, if treated with a few drops of ferric chloride solution, show a marked green colour, changing on being alkaliised by a solution of sodic hydrocarbonate to violet, and then on being acidified by acetic acid, changing back again to green.

* E. Baumann and C. Preuss: *Zeitschrift f. Phys. Chemie*, iii., 156. "Anleitung zur Harn-Analyse." W. F. Löbisch, Leipzig, 1881, pp. 142, 160. Schmiedeberg: *Chem. Cento.* (3), 13, 598.

† *Pflüger's Archiv*, 13, 1876, 289.

According to Thudichum,* the urine of men and dogs, after the ingestion of carbolic acid, contains a blue pigment.

The Action of Carbolic Acid considered physiologically.—Researches on animals have elucidated in a great measure the mode in which carbolic acid acts, and the general sequence of effects, but there is still much to be learnt.

E. Küster † has shown that the temperature of dogs, when doses of carbolic acid in solution are injected subcutaneously, or into the veins, is immediately, or very soon after the operation, raised. With small and moderate doses, this effect is but slight—from half to a whole degree—on the day after the injection the temperature sinks below the normal point, and only slowly becomes again natural. With doses that are just lethal, first a rise and then a rapid sinking of temperature are observed, but with those excessive doses which speedily kill, the temperature at once sinks without a preliminary rise. The action on the heart is not very marked, but there is always a slowing of the cardiac pulsations; according to Hoppe-Seyler the arteries are relaxed. The respiration is much quickened; this acceleration is due to an excitement of the vagus centre, since Salkowsky has shown that section of the vagus produces a retardation of the respiratory wave. Direct application of the acid to muscles or nerves quickly destroys their excitability without a previous stage of excitement. The main cause of the lethal action of carbolic acid—putting on one side those cases in which it may kill by its local corrosive action—appears to be through paralysis of the respiratory nervous centres. The convulsions arise from the spinal cord. On the cessation of the convulsions, the superficial nature of the breathing assists other changes by preventing the due oxidation of the blood.

Carbolic acid is separated from the body, partly by the skin, and partly by the urine as phenyl-sulphuric acid, in combination with alkalies and other compounds already mentioned. It also apparently undergoes other chemical changes, and produces hydroquinones, pyrocatechin, and double ethers. Salkowsky considers that, with rabbits, he has also found oxalic acid in the urine as an oxidation product. According to the researches of Binnendijk,‡ the separation of carbolic acid by the urine commences very quickly after its ingestion; and under favourable circumstances, it may be completely excreted within from twelve to sixteen hours. It must be remembered that the presence of carbolic acid is possible in the animal body, as the result of the digestion of albuminous substances, or of their putrefaction. A small amount of carbolic acid is

* "On the Pathology of the Urine," Lond. 1877, p. 198.

† *Archiv f. Klin. Chirurgie*, Bd. 23. S. 133, 1879.

‡ *Journal de Pharmacie et de Chimie*.

said to be daily excreted by healthy men when feeding on mixed diet; this quantity Engel,* by experiment, estimates to be in the twenty-four hours '015 grm.

Post-mortem Appearances.—No fact is better ascertained from experiments on animals than the following :—that with lethal doses of carbolic acid, administered by subcutaneous injection, or introduced by the veins, no appearances may be found after death which can be called at all characteristic. Further, in the cases in which death has occurred from the outward application of the acid for the cure of scabies, &c., no lesion was ascertained after death which could—apart from the history of the case and chemical evidence—with any confidence be ascribed to a poison.

On the other hand, when somewhat large doses of the acid are taken by the mouth, very coarse and appreciable changes are produced in the upper portion of the alimentary tract. There may be brownish, wrinkled spots on the cheek or lips; the mucous membrane of the mouth, throat, and gullet is often white, and, if the acid was concentrated, eroded. The stomach is sometimes thickened, contracted, and blanched, a condition well shown in a pathological preparation (ix. 206, 43 f) in St. George's Hospital. The mucous membrane, indeed, may be quite as much destroyed as if a mineral acid had been taken. Thus, in Guy's Hospital museum (1799₄₀), there is preserved the stomach of a child who died from taking accidentally carbolic acid. It looks like a piece of paper, and is very white, with fawn-coloured spots; the rugae are absent, and the mucous membrane seems to have entirely vanished. Not unfrequently the stomach exhibits white spots with roundish edges. The duodenum is often affected, and the action is not always limited to the first part of the intestine.

The respiratory passages are often inflamed, and the lungs infiltrated and congested. As death takes place from an asphyxiated condition, the veins of the head and brain, and the blood-vessels of the liver, kidney, and spleen, are gorged with blood, and the right side of the heart distended, while the left is empty. On the other hand, a person may die of sudden nervous shock from the ingestion of a large quantity of the acid, and in such a case the *post-mortem* appearances will not then exhibit precisely the characters just detailed. Putrefaction is retarded according to the dose, and there is often a smell of carbolic acid.[†] If any urine is contained in the bladder, it will probably be dark, and present the characters of carbolic urine detailed at p 152.

* *Annales de Chimie et de Physique*, 5 Ser., T. 20, p. 230, 1880.

† In order to detect this odour, it is well to open the head first, lest the putrefaction of the internal viscera be so great as to mask the odour.

TESTS FOR CARBOLIC ACID.

The Pine-wood Test.—Certain pine-wood gives a beautiful blue colour when moistened, first with carbolic acid, and afterwards with hydrochloric acid, and exposed to the light. Some species of pine give a blue colour with hydrochloric acid alone, and such must not be used; others do not respond to the test for carbolic acid. Hence it is necessary to try the chips of wood first, to see how they act, and with this precaution the test is very serviceable, and, in cautious hands, no error will be made.

Ammonia and Hypochlorite Test.—If to a solution containing even so small a quantity as one part of carbolic acid in 5,000 parts of water, first, about a quarter of its volume of ammonia hydrate be added, and then a small quantity of sodic hypochlorite solution, avoiding excess, a blue colour appears; warming quickens the reaction, the blue is permanent, but turns to red with acids. If there is a smaller quantity than the above proportion of acid, the reaction may be still produced feebly after standing for some time.

Ferric Chloride.—One part of phenol in 3,000 parts of water can be detected by adding a solution of ferric chloride; a fine violet colour is produced. This is also a very good test, when applied to a distillate; but if applied to a complex liquid, the disturbing action of neutral salts and other substances may be too great to make the reaction under those circumstances of service.

Bromine.—The most satisfactory test of all is treatment of the liquid by bromine-water. A precipitate of tri-bromo-phenol ($C_6H_3Br_3O$) is rapidly or slowly formed according to the strength of the solution; in detecting very minute quantities the precipitate must be given time to form. According to Allen,* a solution containing but $\frac{1}{6000}$ of carbolic acid gave the reaction after standing twenty-four hours.

The properties of the precipitate are as follows:—it is crystalline, and under the microscope is seen to consist of fine stars of needles; its smell is peculiar; it is insoluble in water and acid liquids, but soluble in alkalies, ether, and absolute alcohol; a very minute quantity of water suffices to precipitate it from an alcoholic solution; it is therefore essential to the success of the test that the watery liquid to be examined is either neutral or acid in reaction.

Tri-bromo-phenol may be used for the quantitative estimation of carbolic acid, 100 parts of tri-bromo-phenol are equal to 28.39 of carbolic acid; by the action of sodium amalgam tri-bromo-phenol is changed back into carbolic acid.

* "Commercial Organic Analysis," vol. i., p. 306.

That bromine-water precipitates several volatile and fixed alkaloids from their solutions is no objection to the bromine test, for it may be applied to a distillation product, the bases having been previously fixed by sulphuric acid. Besides, the properties of tri-bromo-phenol are distinct enough, and therefore there is no valid objection to the test. It is the best hitherto discovered. There are also other reactions, such as that Millon's reagent strikes a red—molybdic acid, in concentrated sulphuric acid a blue—and potassic dicromate with sulphuric acid a brown colour—but to these there are objections. Again we have the *Euchlorine* test in which the procedure is as follows:—A test-tube is taken, and concentrated hydrochloric acid is allowed to act therein upon potassic chlorate. After the gas has been evolved for from thirty to forty seconds, the liquid is diluted with one and a half volume of water, the gas removed by blowing through a tube, and solution of strong ammonia poured in so as to form a layer on the top; after blowing out the white fumes of ammonium chloride, a few drops of the sample to be tested are added. In the presence of carbolic acid, a rose-red, blood-red, or red-brown tint is produced, according to the quantity present. Carbolic acid may be confounded with *cresol* or with *creasote*, but the distinction between pure carbolic acid, pure cresol, and creasote is plain.

Cresol is at ordinary temperatures a liquid, and cannot be obtained in a crystalline state by freezing. Its boiling point is from 198° to 203°; it is almost insoluble in strong ammonia, and, when sixteen volumes are added, it then forms crystalline scales. On the other hand, carbolic acid is soluble in an equal volume of ammonia, and is then precipitated by the addition of one and a half volume of water. Cresol is insoluble in small quantities of pure six per cent. soda solution; with a large excess, it forms crystalline scales; while carbolic acid is freely soluble in small or large quantities of alkaline solutions.

Cold petroleum spirit dissolves cresol, but no crystalline scales can be separated out by a freezing mixture. Carbolic acid, on the contrary, is but sparingly soluble in cold petroleum, and a solution of carbolic acid in hot petroleum, when exposed to sudden cold produced by a freezing mixture, separates out crystals from the upper layer of liquid. Cresol is miscible with glycerine of specific gravity 1.258 in all proportions; one measure of glycerine mixed with one measure of cresol is completely precipitated by one measure of water. Carbolic acid, under the same circumstances, is not precipitated. The density of cresol is about 1.044. It forms with bromine a tri-bromo-cresol, but this is liquid at ordinary temperatures, while tri-bromo-phenol is solid. On the other hand, it resembles carbolic acid in its reactions with ferric chloride and with nitric and sulphuric acid.

Creasote or *Kreozote* is a term applied to the mixture of crude phe-

nols obtained from the distillation of wood-tar. It consists of a mixture of substances of which the chief are guaiacol or oxyresol ($C_7H_8O_2$), boiling at 200° , and creasol ($C_8H_{10}O_2$) boiling at 217° , also in small quantities of phlorol ($C_8H_{10}O$), methyl creasol ($C_9H_{12}O_2$), and other bodies. Morson's English creasote is prepared from Stockholm tar, and boils at about 217° , consisting chiefly of creasol; it is not easy, by mere chemical tests, to distinguish creasote from cresylic acid. Creasote, in its reactions with sulphuric and nitric acid, bromine and gelatin, is similar to carbolic and cresylic acid, and its solubility in most solvents is also similar. It is, however, distinguished from the tar acids by its insolubility in Price's glycerine, specific gravity 1.258, whether one, two, or three volumes of glycerine be employed. But the best test is its action on an ethereal solution of nitro-cellulose. Creasote mixes freely with the B.P. collodium, while cresylic acid or carbolic acid at once coagulates the latter. With complicated mixtures containing carbolic acid, cresol, and creasote, the only method of applying these tests with advantage is to submit the mixture to fractional distillation.

Flückiger* tests for small quantities of carbolic acid in creasote, by mixing a watery solution of the sample with one-fourth of its volume of ammonia hydrate, wetting the inside of a porcelain dish with this solution, and then carefully blowing bromine fumes on to the surface. A fine blue colour appears if carbolic acid is present, but if the sample consists of creasote only, then it is dirty green or brown. Excess of bromine spoils the reaction.†

Carbolic Acid in Organic Fluids or in the Tissues of the Body.—If the routine process given at page 51, where the organic fluid is distilled

* *Arch. der Pharmacie*, cxiii., p. 30.

† Creasote is, without doubt, poisonous, though but little is known of its action, and very few experiments are on record in which pure creasote has been employed. Eulenberg has studied the symptoms in rabbits, by submitting them to vapourised creasote—*i. e.*, the vapour from twenty drops of creasote diffused through a glass shade under which a rabbit was confined. There was at once great uneasiness, with a watery discharge from the eyes, and after seven minutes the rabbit fell on its side, and was slightly convulsed. The cornea was troubled, and the eyes prominent; a white slime flowed from the mouth and eyes. After fifteen minutes there was narcosis, with lessened reflex action; the temperature was almost normal. There was rattling breathing, and in half an hour the animal died, the respiration ceasing, and fluid blood escaping from the nose. Section after death showed the brain to be hyperæmic, the mucous membranes of the air passages to be covered with a thin layer of fluid blood, and the lungs to be congested; the right side of the heart was gorged with fluid blood.

The *post-mortem* appearances and the symptoms generally are, therefore, closely allied to those produced by carbolic acid. A dark colour of the urine has also been noticed.

in a vacuum after acidifying with tartaric acid, is employed, carbolic acid, if present, will certainly be found in the distillate. If, however, a special search be made for the acid, then the fluid must be well acidified with sulphuric acid, and distilled in the usual way. The distillation should be continued as long as possible, and the distillate shaken up with ether in the apparatus figured at page 135. On separation and evaporation of the ether, the carbolic acid, if present, will be left in a pure enough form to show its reactions. The same process applies to the tissues, which, in a finely-divided state, are boiled, and distilled with dilute sulphuric acid, and the distillate treated as just detailed.

Like most poisons, carbolic acid has a selective attraction for certain organs, so that unless all the organs are examined, it is by no means indifferent which particular portion is selected for the inquiry. Hoppe-Seyler applied carbolic acid to the abdomen and thighs of dogs, and when the symptoms were at their height bled them to death, and separately examined the parts. In one case, the blood yielded .00369 per cent.; the brain, .0034 per cent.; the liver, .00125; and the kidneys, .00423 per cent. of their weight of carbolic acid. The liver then contains only one-third of the quantity found in an equal weight of blood, and, therefore, the acid has no selective affinity for that organ. On the other hand, the nervous tissue, and especially the kidneys, appear to concentrate it.

Examination of the Urine for Carbolic Acid.—It has been previously stated (see p. 152) that the urine will not contain carbolic acid as such, but as a compound salt—viz., phenyl-sulphate of potassium. By boiling with a mineral acid this compound may, however, be broken up, and carbolic acid obtained, either by distillation or by extraction with ether. To detect very minute quantities, a large quantity of the urine should be evaporated down to a syrup, and treated with hydro-chloric acid and ether. On evaporating off the ether, the residue should be distilled with dilute sulphuric acid, and this distillate then tested with bromine-water, and the tri-bromo-phenol collected, identified, and weighed.

Thudichum * has separated crystals of potassic phenyl-sulphate itself from the urine of patients treated endermically by carbolic acid, as follows:—

The urine was evaporated to a syrup, extracted with alcohol of 90 per cent., treated with an alcoholic solution of oxalic acid as long as this produced a precipitate, and then shaken with an equal volume of ether. The mixture was next filtered, neutralised with potassic carbonate, evaporated to a small bulk, and again taken up with alcohol. Some oxalate and carbonate of potassium were separated, and on evaporation to syrup, crystals of potassic phenyl-sulphate were obtained. They gave to analy-

* *Pathology of the Urine*, " p. 193.

sis 46.25 per cent. H_2SO_4 , and 18.1 K—theory requiring 46.2 of H_2SO_4 and 18.4 of K. Alkaline phenyl-sulphates strike a deep purple colour with ferric chloride. To estimate the amount of phenyl-sulphate in the urine, the normal sulphates may be separated by the addition of chloride of barium in the cold, first acidifying with hydrochloric acid. On boiling the liquid a second cup of sulphate is obtained, due to the breaking up of the phenyl-sulphate, and from this second weight the amount of carbolic acid can be obtained— $C_6H_5HSO_4$: $BaSO_4$: : 174 : 233.

Assay of Disinfectants, Carbolic Acid Powders, &c.—For the assay of crude carbolic acid, Mr. Charles Lowe * uses the following process:—A thousand parts of the sample are distilled without any special condensing arrangement; water first comes over, and is then followed by an oily fluid. When a hundred parts of the latter, as measured in a graduated tube, have been collected, the receiver is charged. The volume of water is read off. If the oily liquid floats on the water, it contains light oil of tar; if it is heavier than the water, it is regarded as hydrated acid, containing 50 per cent. of real carbolic acid. The next portion consists of anhydrous cresylic and carbolic acids, and 625 volumes are distilled over; the remainder in the retort consists wholly of cresylic acid and the higher homologues. The relative proportions of carbolic and cresylic acids are approximately determined by taking the solidifying point, which should be between 15.5° and 24°, and having ascertained this temperature, imitating it by making mixtures of known proportions of carbolic and cresylic acids.

E. Waller † has recommended the following process for the estimation of carbolic acid. It is based on the precipitation of the tar acids by bromine, and, of course, all phenols precipitated in this way will be returned as carbolic acid. The solutions necessary are—

1. A solution containing 10 grms. of pure carbolic acid to the litre; this serves as a standard solution.
2. A solution of bromine in water.
3. Solution of alum in dilute sulphuric acid. A litre of 10 per cent. sulphuric acid is shaken with alum crystals until saturated.

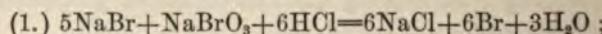
The actual process is as follows:—10 grms. of the sample are weighed out and run into a litre flask, water added, and the mixture shaken. The flask being finally filled up to the neck, some of the solution is now filtered through a dry filter, and 10 cc. of this filtrate is placed in a 6 or 8-ounce stoppered bottle, and 30 cc. of the alum solution added. In a similar bottle 10 cc. of the standard solution of carbolic

* Allen's "Commercial Organic Analysis," vol. i., p. 311.

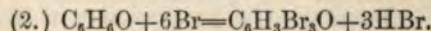
† *Chem. News*, April 1, 1881, p. 152.

acid are placed, and a similar quantity of alum solution is added as in the first bottle. The bromine water is now run into the bottle containing the standard solution of carbolic acid from a burette until there is no further precipitate; The bottle is stoppered and shaken after every addition. Towards the end of the reaction the precipitate forms but slowly, and when the carbolic acid is saturated, the slight excess of bromine water gives the solution a pale yellow tint. The solution from the sample is treated in the same way, and, from the amount of bromine water used, the percentage of the sample is obtained by making the usual calculations. Thus, supposing that 5 cc. of the standard required 15 cc. of the bromine water for precipitation, and 10 cc. of the solution of the sample required 17 cc., the calculation would be $15 \times 2 : 17 = 100 : x$ per cent. With most samples of crude carbolic acid, the precipitate does not readily separate. It is then best to add a little of the precipitate already obtained by testing the standard solution, which rapidly clears the liquid.

Koppeschaar's volumetric method is more exact, but also more elaborate, than the one just described. Caustic normal soda is treated with bromine until permanently yellow, and the excess of bromine is then driven off by boiling. The liquid now contains $5\text{NaBr} + \text{NaBrO}_3$, and on adding this to a solution containing carbolic acid, and a sufficient quantity of hydrochloric acid to combine with the sodium, the following reactions occur:—



and



Any excess of bromine liberated in the first reaction above that necessary for the second, will exist in the free state, and from the amount of bromine which remains free the quantity of carbolic acid can be calculated, always provided the strength of the bromine solution is first known. The volumetric part of the analysis, therefore, merely amounts to the determination of free bromine, which is best found by causing it to react on potassium iodide, and ascertaining the amount of free iodine by titration with a standard solution of sodium thio-sulphate. In other words, titrate in this way the standard alkaline bromine solution, using as an indicator starch paste until the blue colour disappears.

Colorimetric Method of Estimation.—A very simple and ever-ready way of approximately estimating minute quantities of the phenols consists in shaking up 10 grms. of the sample with water, allowing any tar or insoluble impurities to subside. Ten cc. of the clear fluid are then taken, and half a cc. of a 5 per cent. solution of ferric chloride added. The

colour produced is imitated exactly by a standard solution of carbolic acid, and a similar amount of the reagent, on the usual principles of colorimetric analysis.

Carbolic Acid Powders.—Siliceous carbolic acid powders are placed in a retort and distilled. Towards the end the heat may be raised to approaching redness. The distillate separates into two portions—the one aqueous, the other consisting of the acids—and the volume may be read off, if the distillate be received in a graduated receiver. Carbolic acid powders, having lime as a basis, may be distilled in the same way, after first decomposing with sulphuric acid. The estimation of the neutral tar oils in the distillate is easily performed by shaking the distillate with caustic soda solution, which dissolves completely the tar acids. The volume of the oils may be directly read off, if the receiver is a graduated tube. Allen* has suggested the addition of a known volume of petroleum to the distillate, which dissolves the tar oils, and easily separates, and thus the volume may be more accurately determined, a correction being of course made by subtracting the volume of petroleum first added.

Carbolic Acid Soap.—A convenient quantity of soap is carefully weighed, and dissolved in a solution of caustic soda by means of heat. A saturated solution of salt is next added, sufficient to precipitate entirely the soap, which is filtered off; the filtrate is acidified with hydrochloric acid, and bromine water added. The precipitated tri-bromophenol is first melted by heat, then allowed to cool, and the mass removed from the liquid, dried, and weighed.

X.—NITRO-BENZENE.

Nitro-benzene is the product resulting from the action of strong nitric acid on benzene. Its chemical formula is $C_6H_5NO_2$. When pure, it is of a pale yellow colour, of a density of 1.186, and boils at from 205° to 210°. It may be obtained in prismatic crystals by exposure to a temperature of 3°. Its smell is exactly the same as that from the oil or essence of bitter almonds; and it is from this circumstance, under the name of "essence of mirbane," much used in the preparation of perfumes and flavouring agents.

In commerce there are three kinds of nitro-benzene—the purest with the characters given above; a heavier nitro-benzene, boiling at 210° to 220°; and a very heavy variety, boiling at 222° to 235°. The last is specially used

* *Op. Cit.*, i., p. 310.

for the preparation of aniline or aniline blue. Nitro-benzene has been used as an adulterant of bitter almond oil, but the detection is easy (see vol. i, of this work, "Foods," p. 505). Nitro-benzene was first discovered by Mitscherlich in 1834, and its poisonous properties were first pointed out by Casper* in 1859. Its technical use in perfumes, &c., dates from about 1848, and in the twenty-eight years intervening between that date and 1876, Jübell † has collected forty-two cases of poisoning by this agent, thirteen of which were fatal. One of these cases was suicidal, the rest accidental.

Effects of Poisoning by Nitro-Benzene.—Nitro-benzene is a very powerful poison, whether taken in the form of vapour or as a liquid. The action of the vapour on animals has been studied by Eulenberg ‡ and others. One experiment will serve as an illustration. Fifteen grms. of nitro-benzene were evaporated on warm sand under a glass shade, into which a cat was introduced. There was immediately observed in the animal much salivation, and quickened and laboured breathing. After thirty minutes exposure, on removing the shade to repeat the dose of 15 grms., the cat for the moment escaped. On being put back there was again noticed the salivation and running at the eyes, with giddiness and repeated rising and falling. The animal at last, about one hour and forty minutes after the first dose, succumbed with dyspnoea, and died with progressive paralysis of the respiration. The membranes of the brain were found gorged with blood, the lungs liver-coloured, the mucous membrane of the trachea—to the finest subdivisions of the bronchia—reddened, inflamed, and clothed with a fine frothy mucous. The left side of the heart was filled with thick, black blood. The bladder contained 8 grms. of clear urine, in which aniline was discovered. There was a notable smell of bitter almonds.

The effects of the vapour on man are somewhat different in their details to those just described. In a remarkable case related by Dr. Lethaby, a man aged forty-two, had spilt some nitro-benzene over his clothes. He went about several hours breathing an atmosphere of nitro-benzene; he then became drowsy, his expression was stupid, and his gait unsteady, presenting all the appearances of intoxication. The stupor suddenly deepened into coma, and the man died; the fatal course being altogether about nine hours, viz—four hours before coma, and five hours of total insensibility.

An interesting case of poisoning by the vapour is recorded by Tay-

* *Vierteljahrsschrift für Ger. Med.*, 1859, Bd. xvi., p. 1.

† *Die Vergiftungen mit Blausäure u. Nitro-benzol in Forensischer Beziehung*. Erlangen, 1876.

‡ *Gewerbe Hygiene*, S. 607. Berlin, 1876.

lor.* A woman, aged thirty, tasted a liquid used for flavouring pastry, which was afterwards chemically identified as pure nitro-benzene. She immediately spat it out, finding that it had an acrid taste, and probably did not swallow more than a drop. In replacing the bottle, however, she spilt about a tablespoonful, and allowed it to remain for some minutes; it was a small room, and the vapour rapidly pervaded it, and caused illness in herself as well as in a fellow-servant. She had a strange feeling of numbness in the tongue, and in three hours and a quarter after the accident was seen by a medical man; she then presented all the appearances of prussic acid poisoning. The eyes were bright and glassy, the features pale and ghastly, the lips and nails purple, as if stained with blackberries, the skin clammy, and the pulse feeble, but the mind was then clear. An emetic was administered, but she suddenly became unconscious; the emetic acted, and brought up a fluid with an odour of nitro-benzene. The stomach-pump was also used, but the liquid obtained had scarcely any odour of nitro-benzene. In about eleven hours consciousness returned, and in about seventeen hours she partially recovered, but complained of flashes of light and strange colours before her eyes. Recovery was not complete for weeks. In this case, the small quantity swallowed would probably of itself have produced no symptoms, and the effects are to be mainly ascribed to the breathing of the vapour.

The liquid, when swallowed, acts almost precisely in the same way as the vapour, and the symptoms resemble very much those produced by prussic acid. The great distinction between prussic acid and nitro-benzene poisoning is that, in the latter, there is an interval between the taking of the poison and its effects. This is, indeed, one of the strangest phenomena of nitro-benzene poisoning, for the person, after taking it, may appear perfectly well for periods varying from a quarter of an hour to two or three hours, or even longer, and then there may be most alarming symptoms followed by rapid death. Poisoning by nitro-benzene satisfies the ideal of the dramatist, who requires, for the purposes of his plot, poisons not acting at once, but with an interval sufficiently prolonged to admit of lengthy rhapsodies and a complicated dénouement. On drinking the poison there is a burning taste in the mouth, shortly followed by a very striking blueness or purple appearance of the lips, tongue, skin, nails, and even the conjunctivæ. This curious colour of the skin has, in one or two instances, been witnessed an hour before any feeling of illness manifested itself; vomiting then comes on, the vomited matters smelling of nitro-benzene. The skin is cold, there is great depression, and the pulse is small and weak. The respiration is affected, the breathing being slow and irregular, the breath smelling strongly of the liquid, and the odour often persisting for days. A further stage is that of loss of consciousness, and this comes on with all the

* "Poisons," Third Edition, p. 665.

suddenness of a fit of apoplexy. The coma is also similar in appearance to apoplectic coma, but there have frequently been seen trismus and convulsions of the extremities. The pupils are dilated and do not react to light, and reflex sensibility is sometimes completely extinguished. Cases vary a little in their main features; in a few, the blue skin and the deep sleep are the only symptoms noted. Death, for the most part, occurs after a period of from eight to twenty-four hours, (occasionally as soon as four or five hours) after taking the poison.

From the following remarkable train of symptoms in a dog, it is probable, indeed, that nitro-benzene, taken by a human being, might produce death after a rather prolonged period of time, by its secondary effects:—To a half-bred grey-hound* was administered 15 grms. of nitro-benzene, when shortly after there were noticed much salivation, shivering, and muscular twitchings. The same dose was repeated at the end of five, of seven, and of eight hours respectively, so that the dog altogether took 60 grms., but with no other apparent symptom than the profuse salivation. On the following day, the dog voided a tapeworm; vomiting supervened; the heart's action was quickened, and the breathing difficult; convulsions followed, and the pupils were seen to be dilated. For eight days the dog suffered from dyspncea, quickened pulse, shivering of the legs or of the whole body, tetanic spasms, bloody motions, great thirst and debility. The temperature gradually sank under 25°, and the animal finally died. The autopsy showed, as the most striking change, the whole mucous membrane of the intestinal tract covered with a yellow layer, which chemical analysis proved to be caused by picric acid, and in the urine, liver, and lungs, aniline was discovered.

Fatal Dose.—It is probable, from recorded cases, that 1 grm. (15⁴ grain) would be quite sufficient to kill an adult, and, under favourable circumstances, less than that quantity. It would seem that spirituous liquids especially hasten and intensify the action of nitro-benzene, so that a drunken person, *cateris paribus*, taking the poison with spirits, would be more affected than taking it under other conditions.

In a case related by Stevenson,† in which so small a quantity as 1⁷⁴

* Eulenberg, *Gewerbe Hygiène*, S. 607.

† This case is not uninteresting. Through a mistake in reading an extremely illegible prescription, M. S. S., aet. 21, was supplied by a druggist with the following mixture:—

R. Benzole-Nit., 3ij.
Ol. Menth, pep., 3ss.
Ol. Olivæ, 3x.
gutt. xxx., t. ds.

He took on sugar seven doses, each of 20 minims, equalling in all 23 min., (or by weight 27·1 grain, 1·74 grm.) of nitro-benzene, viz., three doses on the first day,

grms. was taken in seven doses, spread over more than forty-eight hours; there were yet extremely alarming symptoms, and the patient seems to have had a narrow escape. The quantity of nitro-benzene which would be fatal, if breathed, is not known with any accuracy.

Pathological Appearances.—The more characteristic appearances seem to be, a dark-brown or even black colour of the blood, which coagulates with difficulty (an appearance of the blood that has even been noticed during life), venous hyperæmia of the brain and its membranes, and general venous engorgement. In the stomach, when the fluid has been swallowed, the mucous membrane is sometimes reddened diffusely, and occasionally shows ecchymoses of a punctiform character.

The essential action of nitro-benzene is of considerable physiological interest. The blood is certainly in some way changed, and gives the spectrum of acid haematin.* Filehne has found that the blood loses, in a great degree, the power of carrying and imparting oxygen to the tissues, and its content of carbon dioxide is also decreased. Thus, the normal amount of oxygen gas which the arterial blood of a hound will give up is 17 per cent.; but in the case of a dog which had been poisoned with nitro-benzene, it sank to 1 per cent. During the dyspnoea from which the dog suffered, the carbon dioxide exhaled was greater than the normal amount, and the arterial blood (the natural content of which should have been 30 per cent. of this gas), only gave up 9 per cent. Filehne seeks to explain the peculiar colour of the skin by the condition of the blood, but the explanation is not altogether satisfactory. Some part of the nitro-benzene, without doubt, is reduced to aniline in the body—an assertion often made, and as often contradicted—but it has been found in too many cases to admit of question. It would also seem from the experiment on the dog (p. 164), that a conversion into picric acid is not impossible. A yellow colour of the skin and conjunctivæ, as if picric-acid-stained, has been noticed in men suffering under slow poisoning by nitro-benzene.

Detection and Separation of Nitro-Benzene from the Animal Tissues.—It is evident from the changes which nitro-benzene may undergo on the second, and one on the morning of the third day. The first two days he was observed to be looking pale and ill, but went on with his work until the seventh dose, which he took on the third day at 9 a. m. About 2 p. m. (or six hours after taking the seventh dose), he fell down insensible, the body pale-blue, and with all the symptoms already described in the text, and usually seen in nitro-benzene poisoning. With suitable treatment he recovered. The next morning, from 8 ounces of urine some nitro-benzene was extracted by shaking with chloroform. (Thos. Stevenson, M. D., in *Guy's Hospital Reports*, MS., vol. xxi., 1876).

* Filehne, W.—“Ueber die Giftwirkungen des Nitrobenzols.” *Arch. für Exper. Pathol. u. Pharm.*, ix. 329.

go that the expert, in any case of suspected nitro-benzene poisoning, must specially look (1) for nitro-benzene, (2) for aniline, and (3) for picric acid. The best general method for the separation of nitro-benzene is to shake up the liquid (or finely divided solid) with light benzoline (petroleum ether), which readily dissolves nitro-benzene. On evaporation of the petroleum ether, the nitro-benzene is left, perhaps mixed with fatty matters. On treating with cold water, the fats rise to the surface, and the nitro-benzene sinks to the bottom; so that, by means of a separating funnel, the nitro-benzene may be easily removed from animal fats. The oily drops, or fine precipitate believed to be nitro-benzene, may be dissolved in spirit and reduced to aniline by the use of nascent hydrogen, developed from iron filings by hydrochloric acid, and the fluid tested with bleaching powder, or, the aniline itself may be recovered by alkalising the fluid, and shaking up with ether in the separation-tube (p. 135), the ether dissolves the aniline, and leaves it, on spontaneous evaporation, as an oily yellowish mass, which, on the addition of a few drops of sodic hypochlorite, strikes a blue or violet-blue—with acids, a rose red—and with bromine, a flesh-red. It gives alkaloidal reactions with such general reagents as platinum chloride, picric acid, &c. Aniline itself may be extracted from the tissues and fluids of the body by petroleum ether, but in any special search it will be better to treat the organs as in Stas' process—that is, with strong alcohol, acidified with sulphuric acid. After a suitable digestion in this menstrua, filter, and then after evaporating the alcohol, dissolve the alcoholic extract in water; alkalise the aqueous solution, and extract the aniline by shaking it up with light benzoline. On separating the benzoline, the aniline will be left, and it may be dissolved in feebly acid water, and the ordinary tests just enumerated tried.

XI.—HYDROCYANIC ACID.

Hydrocyanic Acid.—Hydric cyanide—specific gravity of liquid 0.7058 at 18° C., boiling point 26.5° (80° F.), H₂Cy=27. The anhydrous acid is not an article of commerce, and is only met with in the laboratory. It is a colourless, transparent liquid, and so extremely volatile that, if a drop fall on a glass plate, a portion of it freezes. It has a very peculiar peach-blossom odour, and is intensely poisonous. It reddens litmus feebly and transiently, dissolves red oxide of mercury freely, forms a white precipitate of argentic cyanide when treated with silver nitrate, and responds to the other tests described hereafter.

Medicinal Preparations of Prussic Acid.—The B.P. acid is a watery solution of prussic acid; its specific gravity should be 0.997, and it should contain 2 per cent. of the anhydrous acid; 2 per cent. is also the amount specified in the pharmacopœias of Switzerland and Norway, and in that of Borussica (VI. ed.); the latter ordains, however, a spirituous solution, and the Norwegian an addition of 1 per cent. of concentrated sulphuric acid. The French prussic acid is ordered to be prepared of a strength equalling 10 per cent.

The adulterations or impurities of prussic acid are hydrochloric, sulphuric,* and formic acids. Traces of silver may be found in the French acid, which is prepared from cyanide of silver. Tartaric acid is also occasionally present. Hydrochloric acid is most readily detected by neutralising with ammonia, and evaporating to dryness in a water-bath; the ammonium cyanide decomposes and volatilises, leaving as a saline residue chloride of ammonium. This may easily be identified by the precipitate of chloride of silver, which its solution gives on testing with silver nitrate, and by the deep brown precipitate with Nessler solution. Sulphuric acid is, of course, detected by chloride of barium, formic acid by boiling a small quantity with a little mercuric oxide; if present, the oxide will be reduced, and metallic mercury fall as a grey precipitate. Silver, tartaric acid, and any other fixed impurities are detected by evaporating the acid to dryness, and examining any residue which may be left. It may be well to give the various strengths of the acids of commerce in a tabular form.

	Per cent.
British Pharmacopœia, Switzerland, Norway, and Bor. (vj),	2
France,	10
Vauquelin's Acid,	3.3
Scheele's,	4 to 5*
Riner's,	10
Robiquet's,	50
Schraeder's,	1.5
Duflos',	9
Pfaff's,	10
Koller's,	25

In English commerce, the analyst will scarcely meet with any acid stronger than Scheele's 5 per cent.

Impure oil of bitter almonds contains hydric cyanide in variable quantity, from 5 per cent. up to 14 per cent. There is an officinal pre-

* A trace of sulphuric or hydrochloric acid should not be called an *adulteration*, for it greatly assists the preservation, and therefore makes the acid of greater therapeutic efficiency.

† Strength very uncertain.

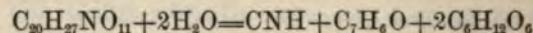
paration obtained by digesting cherry-laurel leaves in water, and then distilling a certain portion over. This *Aqua Lauro-cerasi* belongs to the old school of pharmacy, and is of uncertain strength, but varies from .7 to 1 per cent. of HCN.

Poisoning by Prussic Acid.—Irrespective of suicidal or criminal poisoning, accidents from prussic acid may occur—

1. From the use of the cyanides in the arts.
2. From the somewhat extensive distribution of the acid, or rather of prussic-acid-producing substances in the vegetable kingdom.

1. *In the Arts.*—The galvanic silvering* and gilding of metals, photography, the colouring of black silks, the manufacture of Berlin blue, the dyeing of woollen cloth, and in a few other manufacturing processes, the alkaline cyanides are used, and not unfrequently fumes of prussic acid developed.

2. *In the Vegetable Kingdom.*—A large number of plants contain amygdalin, or bodies formed on the type of amygdalin. In the presence of emulsin (or similar principles) and water, this breaks up into prussic acid and other compounds—an interesting reaction usually represented thus—



1 equivalent of amygdalin—i. e., 457 parts—yielding 1 equivalent of CNH or 27 parts; in other words, 100 parts of amygdalin yield theoretically 5.909 parts of prussic acid,† so that, the amount of either being known, the other can be calculated from it.

The following plants, with many others, all yield, by appropriate treatment, more or less prussic acid:—Bitter almonds, (*Amygdalus communis*) ; the *Amygdalus persica* ; the cherry-laurel (*Prunus lauro-cerasus*) ; the kernels of the plum (*Prunus domestica*) ; the bark, leaves, flowers, and fruit of the wild service-tree (*Prunus padus*) ; the kernels of the common cherry and the apple ; the leaves of the *Prunus capricida* ; the bark of the *Pr. virginiana* ; the flowers and kernels of the *Pr. spinosa* ; the leaves of the *Cerasus acida* ; the bark and almost all

*The preparation used for the silvering of copper vessels is a solution of cyanide of silver in potassic cyanide, to which is added finely powdered chalk. Manipulations with this fluid easily develop hydrocyanic acid fumes, which, in one case related by Martin (*Artzl. Intelligenzbl.*, p. 135, 1872), were powerful enough to produce symptoms of poisoning.

† According to Liebig and Wohler, 17 grms. of amygdalin yield 1 of prussic acid (i. e., 5.7 per cent.) and 8 of oil of bitter almonds. 34 parts of amygdalin, mixed with 66 of emulsin of almonds, give a fluid equalling the strength of acid of most pharmacopœias, viz., 2 per. cent.

parts of the *Sorbus ancuparia*, *S. hybrida* and *S. terminalis*; the young twigs of the *Crataegus oxyacantha*; the leaves and partly also the flowers of the shrubby *Spiræaceæ*, such as *Spirea aruncus*, *S. sorbifolia* and *S. japonica* ;* together with the roots of the bitter and sweet *Cassava*.

In only a few of these, however, has the exact amount of either prussic acid or amygdalin been determined; 1 grm. of bitter almond pulp is about equal to $2\frac{1}{2}$ mgrms. of anhydrous prussic acid. The kernels from the stones of the cherry, according to Geiseler, yield 3 per cent. of amygdalin; therefore, 1 grm. equals 1.7 mgrm. of HCN.

The wild service-tree (*Prunus padus*) and the cherry-laurel (*Prunus Lauro cerasus*) contain, not amygdalin but a compound amygdalin with amygdalic acid; to this has been given the name of lauro-cerasin. It was formerly known as amorphous amygdalin; its formula is $C_{40}H_{55}NO_{24}$; 933 parts are equivalent to 27 of hydric cyanide—that is, 100 parts equal 2.89.

In the bark of the service-tree, Lehmann found 2.7 per cent. of lauro-cerasin (= 0.2 HCN), and in the leaves of the cherry-laurel 1.38 per cent. (= 0.39 HCN).

Francis,† in a recent research on the prussic acid in cassava root, gives as the mean in the sweet cassava 0.0168 per cent., in the bitter 0.0275 per cent., the maximum in each being respectively 0.0238 per cent., and 0.0442 per cent. The bitter fresh cassava root has long been known as a very dangerous poison; but the sweet has hitherto been considered harmless, although it is evident that it also contains a considerable quantity of prussic acid.

The kernels of the peach contain about 2.85 per cent. amygdalin; those of the plum 0.96 per cent. (= 0.56 HCN); and apple pips 0.6 per cent. (= 0.35 per cent. HCN).

It is of great practical value to know, even approximately, the quantity of prussic acid contained in various fruits, since it has been adopted as a defence in criminal cases that the deceased was poisoned by prussic acid developed in substances eaten.

Statistics.—Poisoning by the cyanides (prussic acid or cyanide of potash) occupies the second place among poisons in order of frequency in this country, and accounts for about forty deaths annually.

According to the statistics given on p. 30, in a thousand deaths from poisons of all kinds, two hundred and eighty-nine males and sixty-seven females are likely to die from the cyanides.

In order to ascertain the proportion in which the various forms of commercial cyanides cause death, and also the proportion of accidental,

* The bark and green parts of the *Prunus avium*, L., *Prunus mahaleb*, L., and herbaceous *Spirææ* yield no prussic acid.

† On Prussic Acid from Cassava, *Analyst*, April, 1877, p. 5.

suicidal, and criminal deaths from the same cause, Falck collated twelve years of statistics from medical literature with the following result :—

In fifty-one cases of cyanide poisoning, twenty-nine were caused by potassic cyanide, nine by hydric cyanide, five by oil of bitter almonds, three by peach stones (these three were children, and are classed as "domestic," that is, taking the kernels as a food), three by bitter almonds (one of the three suicidal and followed by death, the other two "domestic"), one by tartaric acid and potassic cyanide (a suicidal case, an apothecary), and one by ferro-cyanide of potassium and tartaric acid. Of the forty-three cases first mentioned, twenty-one were suicidal, seven criminal, eight domestic, and seven medicinal; the forty-three patients were twenty-four men, fourteen children, and five women.

The cyanides are very rarely used for the purpose of murder: a poison which has a strong smell and a perceptible taste, and which also kills with a rapidity only equalled by deadly bullet or knife-wounds, betrays its presence with too many circumstances of a tragic character to find favour in the dark and secret schemes of those who desire to take life by poison. In 793 poisoning cases of a criminal character in France, four only were by the cyanides.

Hydric and Potassic Cyanides were once the favourite means of self-destruction employed by suicidal photographers, chemists, scientific medical men, and others in positions where such means are always at hand; but, of late years the popular knowledge of poisons has increased, and self-poisoning by the cyanides scarcely belongs to a particular class. A fair proportion of the deaths are also due to accident or unfortunate mistakes, and a still smaller number to the immoderate or improper use of cyanide-containing vegetable products.

Accidental, and Criminal Poisoning by Prussic Acid.—The poison is almost always taken by the mouth into the stomach, but occasionally in other ways—such, for example, as in the case of the illustrious chemist, Scheele, who died from inhalation of the vapour of the acid which he himself discovered, owing to the breaking of a flask. There is also the case related by Tardieu, in which cyanide of potassium was introduced under the nails; and that mentioned by Carriere,* in which a woman gave herself, with suicidal intent, an enema containing cyanide of potassium.

With regard to errors in dispensing, the most tragic case on record is that related by Arnold: †—A pharmacist had put in a mixture for

* "Empoisonnement par le cyanure de potassium,—guérison." *Bullet. général de Thérap.*, 1869. No. 30.

† Arnold, A. B. Case of Poisoning by the Cyanide of Potassium. *Amer. Journal of Med. Scien.*, 1869.

a child potassic cyanide instead of potassic chlorate, and the child died after the first dose : the chemist, however, convinced that he had made no mistake, to show the harmlessness of the preparation, drank some of it, and there and then died ; while Dr. Arnold himself, incautiously tasting the draught, fell insensible, and was unconscious for six hours.

Fatal Dose.—Notwithstanding the great number of persons who in every civilised country fall victims to the cyanides, it is yet somewhat doubtful what is the minimum dose likely to kill an adult healthy man. The explanation of this uncertainty is to be sought mainly in the varying strength of commercial prussic acid, which varies from 1·5 (Schraeder's) to 50 per cent. (Robiquet's)—and also in the varying condition of the person taking the poison, more especially whether the stomach be full or empty. In by far the greater number, the dose taken has been much beyond that necessary to produce death, but this observation is true of most poisonings.

The dictum of Taylor, that a quantity of commercial prussic acid, equivalent to 1 English grain (65 mgrm.) of the anhydrous acid would, under ordinary circumstances be sufficient to destroy adult life, has been generally accepted by all toxicologists. The minimum lethal dose of potassic cyanide is similarly put at 2·41 grains (.157 grm.). As to bitter almonds, if it be considered that as a mean they contain 2·5 per cent. of amygdalin, then it would take 45 grms., or about 80 almonds, to produce a lethal dose for an adult ; with children less—in fact, 4–6 bitter almonds are said to have produced poisoning in a child.

Action of Hydric and Potassic Cyanides on Living Organisms.—Both hydric cyanide and potassic cyanide are poisonous to all living forms, vegetable or animal, without exception. The cold-blooded animals take a larger relative dose than the warm-blooded, and the mammalia are somewhat more sensitive to the poisonous action of these cyanides than birds ; but all are destroyed in a very similar manner, and without any essential difference of action. The symptoms produced by hydric and potassic cyanide are identical, and, as regards general symptoms, what is true as to the one is also true as to the other. There is, however, one important difference in the action of these two substances, if the mere local action is considered, for potassic cyanide is very alkaline, possessing even caustic properties. I have seen, e. g., the gastric mucous membrane of a woman, who had taken an excessive dose of potassic cyanide on an empty stomach, so inflamed and swollen, that its state was similar to that induced by a moderate quantity of solution of potash. On the other hand, the acid properties of hydric cyanide are very feeble, and its effect on mucous membranes and the skin in no way resembles that of the mineral acids.

Symptoms observed in Animals.—The main differences between the

symptoms induced in cold-blooded and warm-blooded animals, by a fatal dose or hydric cyanide, are as follows :—

The respiration in frogs is at first somewhat dyspnoeic, then much slowed, and at length it ceases. The heart, at first slowed, later, contracts irregularly, and at length gradually ceases. But all these progressive symptoms are without convulsions. Among warm-blooded animals, on the contrary, convulsions are constant, and the sequence of the symptoms appears to be—dyspnoea, slowing of the pulse, giddiness, falling down, then convulsions with expulsion of the urine and faeces ; dilatation of the pupils, exophthalmus, and finally cessation of the pulse and breathing. The convulsions also frequently pass into general paralysis, with loss of reflex movements, weak, infrequent breathing, irregular, quick, and very frequent pulse, and considerable diminution of temperature.

The commencement of the symptoms in animals is extremely rapid, the rapidity varying according to the dose and the concentration of the acid. It was formerly thought that the death from a large dose of the concentrated acid followed far more quickly than could be accounted for by the blood carrying the poison to the nervous centres ; but Blake was among the first to point out that this doubt was not supported by facts carefully observed, since there is always a sufficient interval between the entry of the poison into the body and the first symptoms to support the theory that the poison is absorbed in the usual manner. Even when Preyer injected a cubic centimetre of 60 per cent. acid into the jugular vein of a rabbit, 29 seconds elapsed before the symptoms commenced. Besides, we have direct experiments showing that the acid—when applied to wounds in limbs, the vessels of which are tied, while the free nervous communication is left open—only acts when the ligature is removed. Magendie describes, in his usual graphic manner, how he killed a dog by injecting into the jugular vein prussic acid, and the “*dog died instantly as if struck by a cannon ball*,” but it is probable that the interval of time was not accurately noted. A few seconds pass very rapidly, and might be occupied even by slowly pressing the piston of the syringe down, and in the absence of accurate measurements, it is surprising how comparatively long intervals of time are unconsciously shortened by the mind. In any case, this observation by Magendie has not been confirmed by the accurate tests of the more recent experimenters ; and it is universally acknowledged that, although with strong doses of hydric cyanide injected into the circulation—or, in other words, introduced into the system—in the most favourable conditions for its speediest action, death occurs with appalling suddenness, yet that it takes a time sufficiently long to admit of explanation in the manner suggested. This has forensic importance, which will be again alluded to. Experiments on animals show

that a large dose of a dilute acid kills quite as quickly as an equivalent dose of a stronger acid, and in some cases it even seems to act more rapidly. If the death does not take place within a few minutes, life may be prolonged for hours, and even, in rare cases, days, and yet the result be death. Coullon poisoned a dog with prussic acid ; it lived for nineteen days, and then died ; but this is quite an exceptional case, and when the fatal issue is prolonged beyond an hour, the chance of recovery is considerable.

The length of time dogs poisoned by fatal doses survive, generally varies from two to fifteen minutes. When the dose is short of a fatal one, these symptoms are as follows :—Evident giddiness and distress ; the tongue is protruded, the breath is taken in short, hurried gasps, there is salivation, and convulsions rapidly set in, preceded, it may be, by a cry. The convulsions pass into paralysis and insensibility. After remaining in this state some time, the animal again wakes up, as it were, very often howls, and is again convulsed ; finally, it sinks into a deep sleep, and wakes up well.

Preyer noticed a striking difference in the symptoms after section of the vagus in animals, which varied according to whether the poison was administered by the lungs, or subcutaneously. In the first case, if the dose is small, the respirations are diminished in frequency ; then, this is followed by normal breathing ; if the dose is larger, there is an increase in the frequency of the respirations. Lastly, if a very large quantity is introduced into the lungs, death quickly follows, with respirations diminished in frequency. On the other hand, when the poison is injected subcutaneously, small doses have no influence on the breathing ; but with large doses, there is an increase in the frequency of the respirations, which sink again below the normal standard.

Symptoms in Man.—When a fatal but not excessive dose of either potassic or hydric cyanide is taken, the sequence of symptoms is as follows :—Salivation, with a feeling of constriction in the throat, nausea, and occasionally vomiting. After a few minutes a peculiar constricting pain in the chest is felt, and the breathing is distinctly affected. Giddiness and confusion of sight rapidly set in, and the person falls to the ground in convulsions similar to those of epilepsy. The convulsions are either general, or attacking only certain groups of muscles ; there is often true trismus, and the jaws are so firmly closed that nothing will part them. The respiration is peculiar, the inspiration is short, the expiration prolonged,* and between the two there is a long interval ever be-

* In a case quoted by Seidel (Maschka's *Handbuch*, p. 321), a man, thirty-six years of age, four or five minutes after swallowing 15 anhydrous HCN in spirits, lay apparently lifeless, without pulse or breathing. After a few minutes was noticed an extraordinary deep expiration, by which the ribs were drawn in almost to the spine, and the chest made quite hollow.

coming more protracted as death is imminent. The skin is pale, or blue, or greyish-blue; the eyes are glassy and staring, with dilated pupils; the mouth is covered with foam, and the breath smells of the poison; the pulse, at first quick and small, sinks in a little while in frequency, and at length cannot be felt. Involuntary evacuation of faeces, urine, and semen is often observed, and occasionally there has been vomiting, and a portion of the vomit has been aspirated into the air-passages. Finally, the convulsions pass into paralysis, abolition of reflex sensibility, and gradual ceasing of the respiration. With large doses these different stages may occur, but the course is so rapid, that they are merged the one into the other, and are undistinguishable. The shortest time between the taking of the acid, and the commencement of the symptoms, may be put at about ten seconds. If, however, a large amount of the vapour is inhaled at once, this period may be rather lessened. The interval of time is so short, that any witnesses generally unintentionally exaggerate, and aver that the effects were witnessed *before* the swallowing of the liquid—"As the cup was at his lips"—"He had hardly drunk it," &c. There is probably a short interval of consciousness, then come giddiness, and, it may be, a cry for assistance; and lastly, there is a falling down in convulsions, and a speedy death. Convulsions are not always present, the victim occasionally appears to sink lifeless at once. Thus, in a case related by Hufeland, a man was seen to swallow a quantity of acid, equivalent to forty grains of the pure acid—that is, about forty times more than sufficient to kill him. He staggered a few paces, and then fell dead, without sound or convulsion.

The very short interval that may thus intervene between the taking of a dose of prussic acid and loss of consciousness, may be utilised by the sufferer in doing various acts, and thus this interval becomes of immense medico-legal importance. The question is simply this:—What can be done by a person in full possession of his faculties in ten seconds? I have found from experiment that, after drinking a liquid from a bottle, the bottle may be corked, the individual can get into bed, and arrange the bedclothes in a suitable manner; he may also throw the bottle away, or out of the window; and, indeed, with practice, in that short time a number of rapid and complicated acts may be performed. This is borne out both by experiments on animals and by recorded cases.

In Mr. Nunneley's numerous experiments on dogs, one of the animals, after taking poison, "went down three or four steps of the stairs, saw that the door at the bottom was closed, and came back again." A second went down, came up, and went again down the steps of a long winding staircase, and a third retained sufficient vigour to jump over another dog, and then leap across the top of a staircase.

In a remarkable case related by Dr. Guy,* in which a young man,

* "Forensic Medicine," 4th Ed., p. 615.

after drinking more wine than usual, was seized by a sudden impulse to take prussic acid, and drank about 2 drachms, producing symptoms which, had it not been for prompt treatment, would, in all probability, have ended fatally—the interval is again noteworthy. After taking the poison in bed, he rose, walked round the foot of a chest of drawers, standing within a few yards of the bedside, placed the stopper firmly in the bottle, and then walked back to bed with the intention of getting into it ; but here a giddiness seized him, and he sat down on the edge, and became insensible.

A case related by Taylor is still stronger. A woman, after swallowing a fatal dose of essence of almonds, went to a well in the yard, drew water, and drank a considerable quantity. She then ascended two flights of stairs and called her child, again descended a flight of stairs, fell on her bed, and died within half an hour from the taking of the poison.

Nevertheless, these cases and similar ones are exceptional, and only show what is possible, not what is usual, the rule being that after fatal doses no voluntary act of significance—save, it may be, a cry for assistance—is performed.

Chronic Poisoning by Hydric Cyanide is said to occur among photographers, gilders, and those who are engaged daily in the preparation or handling of either hydric or potassic cyanides. The symptoms are those of feeble poisoning, headache, giddiness, noises in the ears, difficult respiration, pain over the heart, a feeling of constriction in the throat, loss of appetite, nausea, obstinate constipation, full pulse, with pallor and offensive breath.

Physiological Action of Hydric Cyanide.—Notwithstanding the many researches which have been made with a view to explain fully the action of hydric cyanide, the subject is neither fully exhausted nor elucidated. The symptoms bear a striking analogy to suffocation, or death by asphyxia, and from the changes which occur in the blood (rendering that fluid unfit to carry oxygen to the different parts of the system), it appears probable that in the first instance the respiratory nervous centres are affected, and next, that those fine processes aptly termed “internal respiration,” in which takes place the interchange of oxygen and carbon dioxide between the stationary living cells of the tissues and the moving living cells of the blood, are interfered with. The respiratory centre of the *medulla oblongata* being paralysed, convulsions occur as a natural sequence, but whether the cause of this interference of function is due to hydric cyanide existing as such in the blood, or whether it is due to changes or compounds which hydric cyanide induces in the blood, is a moot question. Preyer considers that hydric cyanide acts directly on the vagus centre, and this is the most probable theory.

Action of Prussic Acid on the Blood.—Hydric cyanide combines

with the haemoglobin of the blood, and is slowly excreted ; it also more than any other poison prevents the exchange of oxygen. If blood saturated with hydrocyanic acid be treated in an absorption-tube with pure oxygen, the gas is not absorbed, nor is the colour of the blood changed ; if blood saturated with oxygen be confined over mercury, and a little hydrocyanic acid in solution be added, there is a gradual development of gas, which is found to consist of oxygen and carbonic anhydride.

Hydric cyanide appears to form a definite crystalline compound with the blood ; and Hoppe-Seyler has observed crystals from blood containing HCN , in which the latter was in such powerful combination, that they crystallised out of warm water. By distillation with an acid, prussic acid was obtained.* Ralph † has described blue masses, like Berlin blue, in the blood, which he considers characteristic of hydrocyanic acid poisoning. Dragendorff has specially looked for this appearance, but has failed to find the blue substance.

According to Schönbein, the blood corpuscles possess the power of decomposing peroxide of hydrogen into water and oxygen ; they lose this property if the blood contains hydrocyanic acid. In the latter case, an addition of peroxide of hydrogen ‡ produces a brown colour with the blood, and causes the spectroscopic bands to disappear. As we have stated, this brown colour is not produced by normal blood. Normal blood again effervesces (owing to the escape of oxygen) when treated with hydric peroxide ; this does not take place with the cyanised blood. Casper speaks very favourably of these characteristics as confirmatory tests in cases of suspected prussic acid poisoning.§ In performing the test with cyanide of potash, the alkali decomposes hydric peroxide, and it is necessary to neutralize with an acid.||

It is not known what becomes of hydric cyanide after ingestion, but it is without doubt in part separated by the lungs and skin in the secretions. It has not indeed been recognized, but it is possible that it decomposes into ammonia and formic acid.

Post-mortem Appearances.¶—If we for the moment leave out of

* *Virchow's Archiv für Path. Anat.*, Bd. 38., p. 435.

† *Journ. of Microscop. Science.* London, New Series, Oct. 24, 1866.

‡ Preoxide of hydrogen is an article of commerce ; should, however, none be at hand, it may be prepared by heating baryta in a current of air, when, by the action of dilute HCl in the peroxide of barium, a solution of H_2O_2 is obtained.

§ *Handbuch*, 6th Ed., p. 497.

|| Judell, *Die Vergiftung mit Blausäure.* Erlangen, 1876.

¶ Hydric cyanide has, according to C. Brame, a remarkable antisectic action, and if administered in sufficient quantity to animals, preserves them after death for a month. He considers that there is some more or less definite combination with the tissues.

consideration any changes which may be seen in the stomach after doses of potassic cyanide, then it may be affirmed that the pathological changes produced by hydric and potassic cyanides mainly coincide with those produced by suffocation. The *post-mortem* appearances in the corpse of an adult suffocated by carbon dioxide and one poisoned by hydric cyanide, will present no difference which can be appreciated by the eye. The lungs and right heart are full of blood, and there is a backward engorgement produced by the pulmonic block. The veins of the neck and the vessels of the head generally are full of blood, and, in like manner, the liver and kidneys are congested. In the mucous membrane of the bronchial tubes there is a bloody foam, the lungs are gorged, and often oedematous in portions; ecchymoses are seen in the pleura and other serous membranes; and everywhere, unless concealed by putrefaction, or some strong-smelling ethereal oil, there is an odour of hydric cyanide.

Casper has rightly recommended the head to be opened and examined first, so as to detect the odour, if present, in the brain. The abdominal and chest cavities usually possess a putrefactive smell, but the brain is longer conserved, so that, if this course be adopted, there is a greater probability of detecting the odour.

The stomach in poisoning by hydric cyanide is not inflamed, but if alcohol has been taken at the same time, or previously, there may be more or less redness.

In poisoning by potassic cyanide, the appearances are mainly the same as those just detailed, with, it may be, the addition of caustic local action. I have, however, seen, in the case of a gentleman who drank accidentally a considerable dose of potassic cyanide just after a full meal, not the slightest trace of any redness, still less of corrosion. Here the contents of the stomach protected the mucous membrane, or possibly the larger amount of acid poured out during digestion sufficiently neutralised the alkali. Potassic cyanide, in very strong solution, may cause erosions of the lips, and the caustic effect may be traced in the mouth, throat, gullet, to the stomach and duodenum; but this is unusual, and the local effects are, as a rule, confined to the stomach and duodenum. The mucous membrane is coloured blood-red, reacts strongly alkaline,* is

* The following case came recently under my own observation:—A stout woman, 35 years of age, the wife of a French-polisher, drank, in a fit of rage, a solution of cyanide of potash. It was estimated that about 15 grains of the solid substance were swallowed. She died within an hour. The face was flushed, the body not decomposed; the mouth smelt strongly of cyanide; the stomach had about an ounce of bloody fluid in it, and was in a most intense state of congestion. There was commencing fatty degeneration of the liver, the kidneys were flabby, and the capsule adherent. The contents of the stomach showed cyanide of potash, and the blood was very fluid. The woman was known to be of intemperate habits.

swollen, and it may be even ulcerated. The upper layers of the epithelium are also often dyed with the colouring-matter of the blood, which has been dissolved out by the cyanide. This last change is a *post-mortem* effect, and can be imitated by digesting the mucous membrane of a healthy stomach in a solution of cyanide. The intensity of these changes are, of course, entirely dependent on the dose and emptiness of the stomach. If the dose is so small as just to destroy life, there may be but little redness or swelling of the stomach, although empty at the time of taking the poison. In those cases in which there has been vomiting, and a part of the vomit has been drawn into the air-passages, there may be also inflammatory changes in the larynx. If essence of almonds has been swallowed, the same slight inflammation may be seen, which has been observed with other essential oils, but no erosion, no strong alkaline reaction, nor anything approaching the effects of the caustic cyanide.

In poisoning by bitter almonds no inflammatory change in the mucous membrane of the coats of the stomach would be anticipated, yet in one recorded case there seems to have been an eroded and inflamed patch.

Tests for Hydrocyanic Acid and Cyanide of Potassium.—(1.) The addition of silver nitrate to a solution containing prussic acid, or a soluble cyanide,* produces a precipitate of argentic cyanide. 100 parts of argentic-cyanide are composed of 80.60 Ag and 19.4 CN, equivalent to 20.1 HCN. It is a white anhydrous precipitate, soluble either in ammonia or in a solution of cyanide of potassium, but insoluble in dilute nitric acid † and water. Upon ignition it is decomposed into CN and metallic silver, mixed with a little paracyanide of silver.

A very neat process for the identification of cyanide of silver is the following:—Place the perfectly dry cyanide in a closed or sealed tube, containing a few crystals of iodine. On heating slightly, iodide of cyanogen is sublimed in beautiful needles. These crystals again may be dissolved in a dilute solution of potash, a little ferrous sulphate added, and hydrochloric acid, and in this way Prussian blue produced. If the quantity to be tested is small, the vapour of the acid may be evolved in a very short test-tube, the mouth of which is closed by the ordinary thin discs of microscopic glass, the under surface of which is moistened with a solution of nitrate of silver; the resulting crystals of silver cyanide are very characteristic, and readily identified by the microscope.

* In the case of testing in this way for the alkaline cyanides, the solution must contain a little free nitric acid.

† It is soluble in hot dilute nitric acid, but separates on cooling. A particle of silver cyanide, moistened with strong ammonia, develops needles; silver chloride treated similarly, octahedral crystals.—(Bloxam).

(2.) If, instead of silver nitrate the disc be moistened with a solution of sulphate of iron (to which has been added a little potash), and exposed to the vapour a short time, and then some dilute hydrochloric acid added, the moistened surface first becomes yellow, then green, lastly, and permanently, blue. No other blue compound of iron (with the exception of Prussian blue) is insoluble in dilute hydrochloric acid.

(3.) A third, and perhaps the most delicate of all, is the so-called sulphur test. A yellow sulphide of ammonium, containing free sulphur, is prepared by saturating ammonia by SH_2 , first suspending in the fluid a little finely-precipitated sulphur (or an old ill-preserved solution of sulphide of ammonium may be used). Two watch-glasses are now taken ; in the one the fluid containing prussic-acid is put, and the second (previously moistened with the sulphide of ammonium described) is inverted over it. The glasses are conveniently placed for a few minutes in the water-oven ; the upper one is then removed, the moist surface evaporated to dryness in the water-bath, a little water added, and then a small drop of solution of chloride of iron. If hydrocyanic acid is present, the sulphocyanide of iron will be formed of a striking blood-red colour.

(4.) The reaction usually called Schönbein's or Pagenstecher and Schönbein's* (but long known,† and used before the publication of their paper,), consists of a guaiacum paper, moistened with a very dilute solution of sulphate of copper (1 : 2,000). This becomes blue if exposed to the vapour of hydrocyanic acid. Unfortunately, the same reaction is produced by ammonia, ozone, nitric acid, hypochlorous acid, iodine, bromine, chromate of potash, and other oxidising agents, so that its usefulness is greatly restricted.

(5.) A very delicate test for prussic acid is as follows :—About one-half centigrm. of ammonia, ferrous sulphate (or other pure ferrous salt) and the same quantity of uranic nitrate, are dissolved in 50 cc. of water, and 1 cc. of this test liquid is placed in a porcelain dish. On now adding a drop of a liquid containing the smallest quantity of prussic acid, a grey-purple colour, or a distinct purple precipitate, is produced.‡

(6.) A hot solution of potassic cyanide, mixed with picric acid, assumes a blood-red colour, due to the formation of picro-cyanic acid. Free HCN does not give this reaction, and therefore must first be neutralised by an alkali.

All these tests, where there is sufficient material, can be directly ap-

* *Neues Report de Pharm.*, 18, 356.

† This reaction (with tincture of guaiacum and copper) has been long known. I remember a pharmacist who attended my father's laboratory, showing me this test in 1828 or 1829."—Mohr's "Toxicologie," p. 92.

‡ M. Casey Lea.—*Amer. Journ. of Science* [3]. ix., p. 121-123 ; *J. C. Society*, 1876, vol. i., p. 112.

plied either to the solution of prussic acid itself, or to that of cyanide of potash ; where necessary, neutralising the one with an alkali, and acidifying the other with an acid—cyanide of potash readily yielding free prussic acid.

Separation of Hydric Cyanide or Potassic Cyanide from Organic Matters, such as the Contents of the Stomach, &c.—It is very necessary, before specially searching for hydric cyanide in the contents of the stomach, to be able to say, by careful and methodical examination, whether there are or are not any fragments of bitter almonds, of apples, peaches, or other substances likely to produce hydric cyanide. If potassic cyanide has been taken, simple distillation will always reveal its presence, because it is found partly decomposed into hydric cyanide by the action of the gastric acids. Nevertheless, an acid should always be added, and if, as in the routine process given at page 51, there is reasonable doubt for suspecting that there will be no cyanide present, it will be best to add tartaric acid (for this organic acid will in no way interfere with subsequent operations), and distil, as recommended, in a vacuum. If, however, from the odour, and from the history of the case, it is pretty sure to be a case of poisoning by hydric or potassic cyanide, then the substances, if fluid, are at once placed in a retort or flask, and acidified with a suitable quantity of sulphuric acid, or if the tissues or other solid matters are under examination, they are finely divided, or pulped, and distilled, after acidifying with sulphuric acid as before. It may be well here, as a caution, to remark that the analyst must not commit the unpardonable error of first producing a cyanide by reagents acting on animal matters, and then detecting as a poison the cyanide thus manufactured. If, for example, a healthy liver is carbonised by nitric acid, saturated with potash, and then burnt up, cyanide of potash is always one of the products ; and, indeed, the ashes of a great variety of nitrogenous organic substances may contain cyanides—cyanides not pre-existing, but manufactured by combination.

The old method of distillation was to distil by the gentle heat of a water-bath, receiving the distillate in a little weak potash water, and not prolonging the process beyond a few hours. The experiments of Sokoloff, however, throw a grave doubt on the suitability of this simple method for quantitative results.

N. Sokoloff* recommends the animal substances to be treated by water strongly acidified with hydric sulphate, and then to be distilled in the water-bath for from two to three days ; or to be distilled for twenty-four hours, by the aid of an oil-bath, at a high temperature. He gives the following example of quantitative analysis by the old process of merely distilling for a few hours, and by the new :—

* *Ber. d. Deutsch. Chem. Gesellsch.* Berlin, ix., p. 1023.

Old Process.—(1.) Body of a hound—age, two years ; weight, 5,180 grms. ; dose administered, 57 mgrms. HCN ; death in fifteen minutes. After five days there was found in the saliva 0·6 mgrm., stomach 3·2 mgrms., in the rest of the intestines, 2·6 mgrms., in the muscles, 4·1—total, 10·5.

(2.) Weight of body, 4,000 grms. ; dose given, 38 mgrms. ; death in eleven minutes. After fifteen days, in the saliva, 0·8, in the stomach, 7·2, in the rest of the intestines, 2·2, in the muscles, 3·2—total, 13·4.

New Process.—Weight of body, 5,700 grms. ; dose, 57 mgrms. ; death in twenty-four minutes. After fifteen days, in the saliva, 1·1 mgrm., in the stomach, 2·6, in the rest of the intestines, 9·6, in the muscles, 31·9, and in the whole, 45·2 mgrms. Duration of process, thirteen hours.

From a second hound, weighing 6,800 grms. ; dose, 67 mgrms. ; 25·1 mgrms. were separated three days after death.

From a third hound, weighing 5,920 grms. ; dose, 98 mgrms. ; after forty days, by distillation on a sand-bath, there were separated 2·8 mgrms. from the saliva, 4·8 from the stomach, 16·8 from the intestines, 23·6 from the muscles—total, 48 mgrms.

It would also appear that he has separated 51·2 mgrms. of anhydrous acid from the corpse of a dog which had been poisoned by 57 mgrms. of acid, and buried sixty days.*

From another canine corpse, three days laid in an oven, and left for twenty-seven days at the ordinary temperature, 5·1 mgrms. were recovered out of a fatal dose of 38 mgrms.

The estimation was in each case performed by titrating the distillate with argentic nitrate, the sulphur compounds having been previously got rid of by saturating the distillate with KHO, and precipitating by lead acetate.

How long after Death can Hydric or Potassic Cyanides be Detected?—Sokoloff† appears to have separated prussic acid from the body of hounds at very long periods after death—in one case sixty days ; Dragendorff recognised potassic cyanide in the stomach of a hound after it had been four weeks in his laboratory,‡ and in man eight days after burial. Casper also, in his 211th case, states that more than 18 mgrms. of anhydrous prussic acid were obtained from a corpse eight days after death.§

* Without wishing to discredit the statements of M. Sokoloff, we may point out that a loss of half a dozen milligrammes only appears rather extraordinary.

† See note above.

‡ Dragendorff, G., *Beitr. zur Gericht. Chem.*, p. 59.

§ Casper's *Prac. Handbuch der Gerichtlichen Medicin*, p. 561.

Dr. E. Tillner* has recognised potassic cyanide in a corpse four months after death. Lastly, Struve† put 300 grms. of flesh, 400 of common water, and 2.378 of KCy in a flask, and then opened the flask after 547 days. The detection was easy, and the estimation agreed with the amount placed there at first. So that even in very advanced stages of putrefaction, and at periods after death extending beyond many months, the detection of prussic acid cannot be pronounced impossible.

Estimation of Hydrocyanic Acid or Potassic Cyanide.—In all cases, the readiest method of estimating prussic acid (whether it be in the distillate from organic substances or in aqueous solution), is to saturate it with soda or potash, and titrate the alkaline cyanide thus formed with nitrate of silver. The process is based on the fact that there is first formed a soluble compound (KCy, AgCy), which the slightest excess of silver breaks up, and the insoluble cyanide is at once precipitated. If grains are used, 17 grains of nitrate of silver are dissolved in water, the solution made up to exactly 1000 grain measures, each grain measure equaling .0054 grain of anhydrous hydrocyanic acid. If grammes are employed, the strength of the nitrate of silver solution should be 1.7 grm. to the litre, each cc. then = .0054 hydrocyanic acid, or .01302 grm. of potassic cyanide.

Essential oil of bitter almonds may also be titrated in this way, provided it is diluted with sufficient spirit to prevent turbidity from separation of the essential oil. If hydrocyanic acid is determined gravimetrically (which is sometimes convenient, when only a single estimation is to be made), it is precipitated as cyanide of silver, the characters of which have been already described.

Case of Poisoning by Bitter Almonds.—Instances of poisoning by bitter-almonds are very rare. The following interesting case is recorded by Maschka:—

A maid-servant, 31 years of age, after a quarrel with her lover, ate a quantity of bitter almonds. In a few minutes she sighed, complained of feeling unwell and faint; she vomited twice, and, after about ten minutes more had elapsed, fell senseless and was convulsed. An hour afterwards, a physician found her insensible, the eyes rolled upwards, the thumb clenched within the shut fists, and the breathing rattling, the pulse very slow. She died within an hour and a half from the first symptoms.

The autopsy showed the organs generally healthy, but all, save the liver, exhaling a faint smell of bitter almonds. The right side of the heart was full of fluid dark blood, the left was empty. Both lungs were rich in blood, which smelt of prussic acid. The stomach was not inflamed—it held 250 grms. of a yellow fluid, containing white flocks smelling of bitter almond oil. In the most dependent portion of the stomach there was a swollen patch of mucous membrane, partially denuded of epithelium. The mucous membrane of the duode-

* *Vierteljahr. f. Gerichtl. Med.* Berlin, 1881, p. 193.

† *Zeitschrift f. Anal. Chemie*, von Fresenius, 1873, xii., p. 4.

num was also swollen and slightly red. The contents of the stomach were acid, and yielded, on distillation, hydride of benzole and hydric cyanide. Residues of the almonds themselves were also found, and the whole quantity taken by the woman from various data was calculated to be 1,200 grains of bitter almonds, equal to 48 grains of amygdalin, or 2·5 grains of pure hydric cyanide.

POISONOUS CYANIDES OTHER THAN HYDRIC AND POTASSIC CYANIDES.

The action of both *sodic and ammonic cyanides* is precisely similar to that of potassic cyanide. With regard to ammonic cyanide, there are several experiments by Eulenberg,* showing that its vapour is intensely poisonous.

A weak stream of ammonic cyanide vapour was passed into glass shades, under which pigeons were confined. After a minute, symptoms of distress commenced, then followed convulsions and speedy death. The *post-mortem* signs were similar to those produced by prussic acid, and this substance was separated from the liver and lungs.

With regard to the *double cyanides*, all those are poisonous from which hydric cyanide can be separated through dilute acids, while those which, like potassic ferro-cyanide, do not admit of this decomposition, may be often taken with impunity, and are only poisonous under certain conditions.

Sonnenschein records the death of a colourist, after he had taken a dose of potassic ferro-cyanide and then one of tartaric acid; and Vol. describes the death of a man, who took potassic ferro-cyanide, and afterwards equal parts of nitric and hydrochloric acids. In this latter case, death took place within the hour, with all the symptoms of poisoning by hydric cyanide; so that it is not entirely true, as most text-books declare, that ferro-cyanide is in no degree poisonous. On the contrary, there are certain conditions in which it may kill speedily.

Mercuric Cyanide, it has been often said, acts precisely like mercuric chloride (corrosive sublimate), and a poisonous action is attributed to it not traceable to cyanogen; but this is erroneous teaching. Bernard † declares that it is decomposed by the gastric juice, and hydric cyanide set free; while Pelikan puts it in the same series as ammonic and potassic cyanides. Lastly, Tolmatscheff,‡ by direct experiment, has found its action to resemble closely that of hydric cyanide.

* *Gewerbe Hygiène*, p. 385.

† *Substances Toxicques*, pp. 66-103.

‡ *Enige Bemerkungen über die Wirkung von Cyanqueck-Silber*, in *Hoppe-Seyler's Med. Chem. Untersuchungen*, 2 Heft, p. 279.

Silver Cyanide acts, according to the experiments of Nunneley, also like hydric cyanide, but very much weaker.

Hydric Sulphocyanide in very large doses is poisonous.

Potassic Sulphocyanide, according to Dubreuil and Legros,* if subcutaneously injected, causes first local paralysis of the muscles, and later, convulsions.

Cyanogen Chloride (CNCl) and also the compound ($\text{C}_5\text{N}_5\text{Cl}_5$)—the one a liquid, boiling at 15° , the other a solid, which may be obtained in crystals—are both poisonous, acting like hydric cyanide.

Methyl Cyanide is a liquid obtained by distillation of a mixture of calcic methyl sulphate and potassic cyanide. It boils at 77° , and is intensely poisonous. Eulenberg† has made with this substance several experiments on pigeons. An example of one will suffice:—A young pigeon was placed under a glass shade, into which methyl cyanide vapour, developed from calcic methyl sulphate and potassic cyanide was admitted. The pigeon became immediately restless, and the faeces were expelled. In forty seconds it was slightly convulsed, and was removed after a few minutes' exposure. The pupils were then observed not to be dilated, but the respiration had ceased; the legs were feebly twitching; the heart still beat, but irregularly; a turbid white fluid dropped out of the beak, and after six minutes, life was extinct.

The pathological appearances were as follows:—In the beak much watery fluid; the membranes covering the brain weakly injected; the *plexus venosus spinalis* strongly injected; in the region of the cervical vertebra a small extravasation between the *dura mater* and the bone; the right lung of a clear cherry-red colour, and the left lung partly of the same colour, the parenchyma presented the same hue as the surface; on section of the lungs a whitish froth exuded from the cut surface. In the cellular tissue of the trachea, there were extravasations 5 mm. in diameter; the mucous membrane of the air-passages was pale; the right ventricle and the left auricle of the heart were filled with coagulated and fluid dark-red blood; liver and kidneys normal; the blood dark-red, and very fluid, becoming bright cherry-red on exposure to the air; blood corpuscles unchanged. Cyanogen was separated, and identified from the lungs and the liver.

Cyanuric Acid ($\text{C}_3\text{O}_3\text{N}_3\text{H}_5$), one of the decomposition-products obtained from urea, is poisonous, the symptoms and pathological effects closely resembling those due to hydric cyanide. In experiments on animals, there has been no difficulty in detecting prussic acid in the lungs and liver after poisoning by cyanuric acid.

* *Compt. Rend.* t. 64, 1867, p. 561.

† *Gewerbe Hygiène*, p. 392.

XII.—PHOSPHORUS.

Phosphorus.—Atomic weight, 31, specific gravity, 1.77 to 1.840. Phosphorus melts at from 44.4° to 44.5° to a pale yellow oily fluid. The boiling point is about 290°.

The phosphorus of commerce is usually preserved under water in the form of waxy, semi-transparent sticks; if exposed to the air, white fumes are given off, luminous in the dark, with a peculiar onion-like odour. On heating phosphorus it readily inflames, burning with a very white flame.

At 0° phosphorus is brittle; the same quality may be imparted to it by a mere trace of sulphur. Phosphorus may be obtained in dodecahedral crystals by slowly cooling large melted masses. It may also be obtained crystalline by evaporating a solution in bisulphide of carbon, or hot naphtha in a current of carbon dioxide. It is usually stated to be absolutely insoluble in water, but Julius Hartmann * contests this, having found in some experiments that 100 grms. of water digested with phosphorus for 64 hours at 38.5° dissolved .000227 grm. He also investigated the solvent action of bile, and found that 100 grms. of bile, under the same conditions, dissolved .02424 grm., and that the solubility of phosphorus rose both in water and bile when the temperature was increased. Phosphorus is somewhat soluble in alcohol and ether, and also, to some extent, in fatty and ethereal oils; but the best solvent is carbon disulphide.

The following is the order of solubility in certain menstrua, the figures representing the number of parts by weight of the solvent required to dissolve one part of phosphorus:—

Carbon Disulphide,	4
Almond Oil,	100
Concentrated Acetic Acid,†	100
Ether,	250
Alcohol, Specific Gravity .822,	400
Glycerine,	588

Phosphorus exists in, or can be converted into, several allotropic modifications, of which the red or amorphous phosphorus is the most important. This is effected by heating it for some time, in the absence of

* *Zur acuten Phosphor-Vergiftung.* Dorpat, 1866.

† Phosphorus is very little soluble in cold acetic acid, and the solubility given is only correct when the boiling acid acts for some time on the phosphorus.

air, from 230° to 235° . It is not poisonous.* Commercial red phosphorus does, however, contain very small quantities of unchanged or ordinary phosphorus—according to Fresenius, from 6 per cent. downwards; it also contains phosphorus acid, and about 4.6 per cent. of other impurities, among which is graphite.†

Phosphuretted Hydrogen.—*Phosphine* (PH_3), mol. weight, 34, specific gravity, 1.178, percentage composition, phosphorus 91.43, hydrogen 8.57 by weight. The absolutely pure gas is not spontaneously inflammable, but that made by the ordinary process is so. It is a colourless, highly-poisonous gas, which does not support combustion, but is itself combustible, burning to phosphoric acid ($\text{PH}_3 + 2\text{O}_2 = \text{PO}_4\text{H}_2$). Extremely dangerous explosive mixtures may be made by combining phosphine and air or oxygen. Phosphine, when quite dry, burns with a white flame, but if mixed with aqueous vapour, it is green; hence a hydrogen flame containing a mixture of PH_3 possesses a green colour.

If sulphur is heated in a stream of phosphine, hydric sulphide and sulphur phosphide are the products. Oxides of the metals, heated with phosphine, yield phosphides with formation of water. Iodine, warmed in phosphine, gives white crystals of iodine phosphonium, and biniodide of phosphorus, $5\text{I} + 4\text{PH}_3 = 3\text{PIH}_2 + \text{PI}_2$. Chlorine inflames the gas, the final result being hydric chloride and chloride of phosphorus, $\text{PH}_3 + 8\text{Cl} = 3\text{ClH} + \text{PCl}_5$. One of the most important decompositions for our purpose is the action of phosphine on a solution of nitrate of silver; there is a separation of metallic silver, and nitric and phosphoric acids are found in solution, thus, $8\text{AgNO}_3 + \text{PH}_3 + 4\text{OH}_2 = 8\text{Ag} + 8\text{HNO}_3 + \text{PO}_4\text{H}_2$. The excess of silver can be separated by hydric chloride, and the phosphoric acid made evident by the addition of molybdic acid in excess—a test which is one of the best we have for phosphine, and hence for phosphorus.

The Medicinal Preparations of Phosphorus are not numerous; it is usually prescribed in the form of pills, often made by manufacturers of coated pills on a large scale. Besides pills, there is a *phosphorated oil*; that of the French pharmacopœia is made with 1 part of dried phosphorus dissolved in 50 parts of warm almond oil; that of the German has 1 part in 80; the strength of the former is therefore 2 per cent., of the latter 1.25 per cent.

Matches and Vermin Pastes.—An acquaintance with the percentage of phosphorus in the different pastes and matches of commerce will be found useful. Most of the vermin-destroying pastes contain from 1 to 2 per cent. of phosphorus.

* A hound took 200 grms. of red phosphorus in twelve days, and remained healthy.—*Sonnenschein*.

† Schrötter: *Chem. News*, vol. xxxvi., p. 198.

A phosphorus paste that was fatal to a child * and gave rise to serious symptoms in others, was composed as follow :—

	Per cent.
Phosphorus,	1·4
Flowers of Sulphur,	42·2
Flour,	42·2
Sugar,	14·2
	—
	100·00

Three common receipts give the following proportions :—

	Per cent.
Phosphorus,	1·5
Lard,	18·4
Sugar,	18·4
Flour,	61·7
	—
	100·0

	Per cent.
Phosphorus,	1·2
Warm Water,	26·7
Rye Flour,	26·7
Melted Butter,	26·7
Sugar,	18·7
	—
	100·00

	Per cent.
Phosphorus,	1·6
Nut Oil,	15·7
Warm Water,	31·5
Flour,	31·5
Sugar,	19·7
	—
	100·00

A very common phosphorus paste, to be bought everywhere in England, is sold in little pots ; the whole amount of phosphorus contained in these, varies from .324 to .388 grm. (5 to 6 grns), the active constituent being a little over 4 per cent. Matches differ much in composition. Six match-heads, which had been placed in an apple for criminal purposes, and were submitted to Tardieu, were found to contain 20 mgrms. of phosphorus, *i.e.*, .33 grm. in 100. Mayet found in a hundred matches 55 mgrms. of phosphorus. Gonning † analysed ten

* Casper's 204th case.

† *Nederlandsch Tijdschr. voor Geneesk.* Afol. i., 1866.

different kinds of phosphorus matches with the following result:—Three English samples contained in 100 matches 34, 33, and 32 mgrms. of phosphorus; a Belgian sample, 38 mgrms.; and five others of unknown origin, 12, 17, 28, 32, and 41 mgrms. respectively. Some of the published formularies are as follows:—

(1.) Glue,	6 parts.
Phosphorus,	4 " or 14·4 per cent.
Nitre,	10 "
Red Ochre,	5 "
Blue Smalts,	2 "
(2.) Phosphorus,	9 parts, or 16·3 per cent.
Gum,	16 "
Nitre,	14 "
Smalts,	16 "
(3.) Phosphorus,	4 parts, or 14·4 per cent.
Glue,	6 "
Nitre,	10 "
Red Lead,	5 "
Smalts,	2 "
(4.) Phosphorus,	17 parts, or 17 per cent.
Glue,	21 "
Nitre,	38 "
Red Lead,	24 "

Phosphorus-poisoning by matches will, however, shortly become very rare, for those containing the ordinary variety of phosphorus are gradually being superseded by matches of excellent quality, which contain no phosphorus whatever.

Statistics.—According to the Registrar-General's mortality returns for the five years, 1876–1880, phosphorus occupies the eleventh place in the order of frequency among deaths from all poisons. In those five years it caused the death of 17 males and 29 females, total 46—a number perhaps equal to about 60 cases. The total deaths in the same period from all poisons (omitting those from poisonous fungi, putrid shell-fish, and the like) were 1,581. It follows, that deaths from phosphorus-poisoning accounted for 29 per thousand of deaths from poisoning by all causes. The ages of the 46 persons whose deaths are recorded fell into the following groups:—

Ages—Years.	-5	5-	10-	15-	20-	25-	35-	45-	55-	65-	Total.
Deaths from Phosphorus Poisoning.	24	2	1	4	1	7	1	4	1	1	46

Therefore, 27 (or rather more than half) were children, and 19 were adults. Fourteen out of the 19 adults took phosphorus for the purpose of suicide, all the other cases were due either to accident or negligence.

A far greater number of cases of poisoning by phosphorus occur yearly in France and Germany than in England. Phosphorus may be considered as the favourite poison, which the common people on the Continent employ for the purpose of self-destruction. It is an agent within the reach of any one who has two sous in his pocket, wherewith to buy a box of matches; but to the educated, and to those who know the horrible and prolonged torture ensuing from a toxic dose of phosphorus, such a means of exit from life will never be favoured.

Otto Schraube* has collected 92 cases from Meischner's work,† and added 16 which had come under his own observation, giving in all 108 cases. Seventy-one (or 65 per cent.) of these were suicidal—of the suicides, 24 were males, 47 females (12 of the latter being prostitutes); 21 of the cases were those of murder, 11 were accidental, and in 3 the cause was not ascertained. The number of cases in successive years, and the kind of poison used, is given as follows:—

Number of Cases.	In the Years.	Phosphorus in Substance or as Paste.	Phosphorus Matches.
15	1798-1850	13	2
36	1850-1860	15	21
41	1860-1864	6	35
16	1864-1867	5	11

Of the 108 cases, 1^o persons recovered and 90 (or 83·3 per cent.) died.

Falck has also collected 76 cases of poisoning from various sources during the last eleven years; 55 were suicidal, 5 homicidal† (murders), and the rest accidental. Of the latter, 2 were caused by the use of phosphorus as a medicine, 13 by accidents due to phosphorus being in the house; in one case phosphorus was taken intentionally to try the effect of an antidote.‡ With regard to the form in which the poison was taken 2 of the 76, as already mentioned, took it as prescribed by physicians, the remaining 74 were divided between poisonings by phosphorus paste

* Schmidt's *Jahrbücher der Ger. Med.*, 1867. Bd. 186, S. 209-248.

† *Die acute Phosphorose und einige Reflexionen über die acute gelbe Leberatrophie, &c.*, Inaug. Diss. Leipzig, 1864.

‡ Dr. Dannenberg has shown by direct experiment that a poisonous dose of phosphorus may be introduced into spirits or coffee, and the mixture have but little odour or taste of phosphorus.—Schuchardt in Maschka's *Handbuch*.

§ Géry, "Uber Terpentinnessenz als Gegenmittel gegen Phosphor," in *Gaz. Hebdo. de Med.*, 2 Ser., x., 2, 1873.

(22) and matches (52) = 70 per cent. Of the 76 cases, 6 were children, 43 adult males, 13 adult females, and 14 adults, sex not given. Of the 76 cases, 42 or 55·3 per cent. died—a much smaller rate of mortality than that shown by Schraube's collection.

Fatal Dose.—The smallest fatal dose on record is that mentioned by Lobenstein Lobel, of Jena, where a lunatic died from taking 7·5 mgrms. (·116 grain). There are other cases clearly indicating that this small quantity may produce dangerous symptoms in a healthy adult.

Effects of Phosphorus.—Phosphorus is excessively poisonous, and will destroy life, provided only that it enters the body in a fine state of division, but, if taken in coarse pieces, no symptoms may follow, for it has been proved that single lumps of phosphorus will go the whole length of a dog's intestinal canal without causing appreciable loss of weight, and without destroying life.* Magendie injected *oleum phosphoratum* into the veins, and although the animals experimented on exhaled white fumes, and not a few died asphyxiated, yet no symptoms of phosphorus poisoning resulted—an observation confirmed by others—the reason being that the phosphorus particles in a comparatively coarse state of division were arrested in the capillaries of the lung, and may be said to have been, as it were, outside the body. On the other hand, A. Brunner,† working in L. Hermann's laboratory, having injected into the veins phosphorus in such a fine emulsion that the phosphorus could pass the lung capillaries, found that there were no exhalations of white fumes, but that the ordinary symptoms of phosphorus poisoning soon manifested themselves. Phosphorus paste, by the method of manufacture, is in a state of extreme sub-division, and hence all the phosphorus pastes are extremely poisonous.

In a few poisons there is a difference, more or less marked, between the general symptoms produced on man, and those noticeable in the different classes of animals; but with phosphorus, the effects on animals appear to agree fairly with those witnessed most frequently in man. Tardieu (who has written perhaps the best and most complete clinical record of phosphorus poisoning extant) divides the cases under three classes, and to use his own words: "I think it useful to establish that poisoning by phosphorus in its course, sometimes rapid, sometimes slow, exhibits in its symptoms three distinct forms—a common form, a nervous form, and a haemorrhagic form. I recognise that, in certain cases, these three forms may succeed each other, and may only constitute periods of poisoning, but it is incontestable that each of them may show itself alone, and occupy the whole course of the illness produced by the

* Reveil, *Ann. d'Hygiène Publ.* (3), xii., p. 370.

† *Arch. f. d. Ges. Physiologie*, iii., p. 1.

poison."* Premising that the common form is a blending of irritant, nervous, and haemorrhagic symptoms, I adopt here in part Tardieu's division. The name of "haemorrhagic form" may be given to that in which haemorrhage is the predominant feature, and the "nervous" to that in which the brain and spinal cord are from the first affected. There yet remain, however, a few cases which have an entirely anomalous course, and do not fall under any of the three classes.

From a study of 121 recorded cases of phosphorus poisoning, I believe the relative frequency of the different forms to be as follows:—The common form, 83 per cent., haemorrhagic, 10 per cent., nervous, 6 per cent., anomalous, 1 per cent. The "anomalous" are probably over-estimated, for the reason that cases presenting ordinary features are not necessarily published, but others are nearly always chronicled in detail.

Common Form.—At the moment of swallowing, a disagreeable taste and smell are generally experienced, and there may be immediate and intense pain in the throat, gullet, and stomach, and almost immediate retching and vomiting. The throat and tongue also may become swollen and painful; but in a considerable number of cases the symptoms are not at once apparent, but are delayed from one to six hours—rarely longer. The person's breath may be phosphorescent before he feels in any way affected, and may go about his business and perform a number of acts requiring both time and mental integrity. Pain in the stomach (which, in some of the cases, takes the form of violent cramp and vomiting) succeeds; the matters vomited may shine in the dark, and are often tinged with blood. Diarrhoea is sometimes present, sometimes absent; sleeplessness for the first night or two is very common. The pulse is variable, sometimes frequent, sometimes slow; the temperature in the morning is usually from 36.0° to 36.5°, in the evening 37° to 38°.

The next symptom is jaundice. I have notes of the exact occurrence of jaundice, in 23 cases, as follows:—In 1 within twenty-four hours, in 3 within thirty-six hours, in 3 within two days, in 11 within three days, in 1 within four days, in 1 within five days, in 1 within nine days, in 1 within eighteen days, and in 1 within twenty-seven days; so that in about 78 per cent. jaundice occurred before the end of the third day. Out of 26 cases, in which the patients lived long enough for the occurrence of jaundice, in 3 (or 11 per cent.) it was entirely absent. In 132 cases recorded by Lewin, Meischner, and Heisler, jaundice occurred in 65, or about 49 per cent., but it must be remembered, that in many of these cases the individual died before it had time to develop. The jaundice having thoroughly pronounced itself, the system may be considered as not only under the influence of the toxic action of phosphorus,

* *Étude Medico-Légale et Clinique sur l'Empoisonnement.* Paris, 1875, p. 483.

but as suffering in addition from all the accidents incidental to the retention of the biliary secretion in the blood ; nor is there from this point any special difference between phosphorus poisoning and certain affections of the liver—such, for example, as acute yellow atrophy. There is retention of urine, sleeplessness, headache, frequent vomiting, painful and often involuntary evacuations from the bowels, and occasionally skin affections, such as urticaria or erythema. The case terminates either by acute delirium with fever, followed by fatal coma, or, in a few instances, coma comes on, and the patient passes to death in sleep without delirium. In this common form there is in a few cases, at the end of from twenty-four to thirty hours, a remission of the symptoms, and a non-medical observer might imagine that the patient was about to recover without further discomfort ; but then jaundice supervenes, and the course is as described. Infants often do not live long enough for the jaundiced stage to develop, but die within twenty-four hours, the chief symptoms being vomiting and convulsions.

Hæmorrhagic Form.—The symptoms set in as just detailed, and jaundice appears, but accompanied by a new and terrible train of events —viz., great effusion of blood. In some cases the blood has been poured out simultaneously from the nose, mouth, bladder, kidneys, and bowels. Among women there is excessive menorrhagia. The liver is found to be swollen and painful ; the bodily weakness is great. Such cases are usually of long duration, and a person may die months after taking the poison from weakness, anaemia, and general cachexia. In many of its phases the hæmorrhagic form resembles scurvy, and as in scurvy there are spots of purpura all over the body.

The Nervous Form is less common than the two forms just described. From the beginning, there are strange creeping sensations about the limbs, followed by painful cramps, repeated faintings, and great somnolence. Jaundice, as usual, sets in, erythematous spots appear on the skin, and, about the fifth day, delirium of an acute character breaks out, and lock-jaw and convulsions close the scene.

The following are one or two brief abstracts of anomalous cases in which symptoms are either wanting, or run a course entirely different from any of the three forms described :—

A woman, aged twenty, took about 3 grains of phosphorus in the form of rat-paste. She took the poison at six in the evening, behaved according to her wont, and sat down and wrote a letter to the king. During the night she vomited once, and died the next morning at six o'clock, exactly twelve hours after taking the poison. There appear to have been no symptoms whatever, save the single vomiting, to which may be added that in the course of the evening her breath had a phosphorus odour and was luminous.*

* Casper's 205th case.

A girl swallowed a quantity of phosphorus paste, but there were no marked symptoms until the fifth day, on which there was sickness and purging. She died on the seventh day. A remarkable blueness of the finger nails was observed a little before death and was noticeable afterwards.*

Sequelæ.—In several cases in which the patients have recovered from phosphorus poisoning, there have been observed paralytic affections.† O. Bollinger has recorded a case in which paralysis of the foot followed ;‡ in another, published by Bettelheim,§ there were peculiar cerebral and spinal symptoms. Most of these cases are to be explained as disturbance or loss of function from small haemorrhages in the nervous substance.

Period at which the first Symptoms commence.—The time when the symptoms commence is occasionally of importance from a forensic point of view. I find that out of 28 cases in which the commencement of evident symptoms—*i. e.*, pain, or vomiting, or illness—is precisely recorded, in 8 the symptoms were described as either immediate or within a few minutes after swallowing the poison ; in 6 the symptoms commenced within the hour ; in 3 within two hours ; in other 3 within four hours ; and in 1 within six hours. One was delayed until the lapse of twelve hours, 1 from sixteen to eighteen hours, 1 two, and another five days. We may, therefore, expect that in half the cases which may occur, the symptoms will commence within the hour, and more than 80 per cent. within six hours.

Period of Death.—In 129 cases death took place as follows :—In 17 within twenty-four hours, in 30 within two days, in 103 within seven days. Three patients lived eight days, 6 nine days, 13 ten days, 1 eleven days, 1 sixteen days, 1 seventeen days, and 1 survived eight months. It hence follows that 79.8 per cent. of the fatal cases die within the week.

Phosphorus Vapour.—There are one or two cases on record of acute poisoning by phosphorus in the form of vapour. The symptoms are somewhat different from the effects produced by the finely-divided solid, and in general terms it may be said that phosphorus vapour is more apt to produce the rarer “nervous” form of poisoning than the solid phosphorus.

Bouchardat || mentions the case of a druggist who, while preparing

* Taylor on “Poisons,” p. 277.

† See Gallavardin, *Les Paralyses Phosphoriques*. Paris, 1865.

‡ *Deutches Archiv f. Klin. Med.*, Bd. 6, Hft. 1, S. 94, 1869.

§ *Wiener Med. Presse*, 1868, No. 41.

|| *Annuaire de Thérap.*, 1874, p. 109. Schuchardt in Maschka’s *Handbuch* ; also Schmidt’s *Jahrbuch*, 1846, Bd. 51, S. 101.

a large quantity of rat-poison in a close room, inhaled phosphorus vapour. He fainted repeatedly, fell into a complete state of prostration, and died within a week.

The following interesting case came under the observation of Professor Magnus Huss:—A man, thirty-nine years old, married, was admitted into the Seraphin-Lazareth, Stockholm, on the 2nd of February, 1842. He had been occupied three years in the manufacture of phosphorus matches, and inhabited the room in which the materials were preserved. He had always been well-conducted in every way, and in good health until a year previously, when a large quantity of the material for the manufacture of the matches accidentally caught fire and exploded. In his endeavours to extinguish the flames, he breathed a large quantity of the vapour, and he fell for a time unconscious. The spine afterwards became so weak that he could not hold himself up, and he lost, in a great measure, power over his legs and arms. On admission, his condition was as follows:—He could make a few uncertain and staggering steps, his knees trembled, his arms shook, and if he attempted to grasp anything when he lay in bed, there were involuntary twitchings of groups of muscles. There was no pain; the sensibility of the skin was unchanged; he had formication in the left arm; the spine was neither sensitive to pressure, nor unusually sensitive to heat (as, e.g., to the application of a hot sponge); the organs of special sense were not affected, but his speech was somewhat thick. He lived to 1845 in the same condition, but the paralysis became worse. There does not seem to have been any autopsy.

The effects of phosphorus vapour may be still further elucidated by one of Eulenberg's* experiments on a rabbit. The vapour of burning phosphorus, mixed with much air, was admitted into a wooden hutch in which a strong rabbit sat. After 5 mgrms. of phosphorus had been in this manner consumed, the only symptoms in half an hour were salivation, and quickened and somewhat laboured respiration. After twenty-four hours had elapsed there was sudden indisposition, the animal fell as if lifeless, with the hind extremities stretched out, and intestinal movements were visible; there was also expulsion of the urine. These epileptiform seizures seem to have continued more or less for twelve days, and then ceased. After fourteen days the experiment was repeated on the same rabbit. The animal remained exposed to the vapour for three quarters of an hour, when the epilepsy showed itself as before, and, indeed, almost regularly after feeding. Between the attacks the respiration was slowed. Eight weeks afterwards there was an intense icterus, which disappeared at the end of ten weeks.

Chronic Phosphorus Poisoning has frequently been noticed in per-

* *Gewerbe Hygiène*, p. 255.

sons engaged either in the manufacture of phosphorus or in its technical application. Some have held that the symptoms are due to an oxidation product of phosphorus rather than to phosphorus itself, but in one of Eulenberg's experiments, in which a dove was killed by breathing phosphorus fumes evolved by phosphorus oil, phosphorus was chemically recognised in the free state in the lungs. The most constant and peculiar effect of breathing small quantities of phosphorus vapour is a necrosis of the lower jaw. There is first inflammation of the periosteum of the jaw, which proceeds to suppuration and necrosis of a greater or smaller portion. The effects may develop with great suddenness, and end fatally. Thus Fournier and Olliver* relate the case of a girl, fourteen years old, who, after working four years in a phosphorus manufactory, was suddenly affected with periostitis of the upper jaw, and with intense anaemia. An eruption of purpuric spots ensued, and she died comatose. There is now little doubt that minute doses of phosphorus have a specific action on the bone generally, and more especially on the bones of the jaw. Wegner † administered small daily doses to young animals, both in the state of vapour, and as a finely-divided solid. The condition of the bones was found to be more compact than normal, the medullary canals being smaller than in healthy bone, the ossification was quickened. The formation of callus in fractured limbs was also increased.

Changes in the Urinary Secretion.—It has been before stated that, at a certain period of the illness, the renal secretion is scantier than in health, the urine diminishing, according to Lebert and Wyss's ‡ researches, to one-half on the third, fourth, or fifth day. It frequently contains albumen, blood, and casts. When jaundice is present, the urine has then all the characters noticed in icterus; leucin and tyrosin, always present in acute yellow atrophy of the liver, have been found in small quantity in jaundice through phosphorus; lactic acid is also present. The urea is much diminished, and, according to Schultzen and Riess, § may be towards death entirely absent. Lastly, it is said that there is an exhalation of either phosphorus vapour or phosphine from such urine (see p. 206).

Changes in the Blood during life have been several times observed. In a case attended by M. Romellære of Brussels, || in which a man took the paste from 300 matches, and under treat-

* *Gaz. hebd. de Méd.*, 29, p. 461., 1868.

† *Virchow's Arch. f. Path. Anat.*, iv., 11.

‡ *Archiv Générale de Méd.*, 6 Sér., Tom. 12, 1868, p. 709.

§ *Annalen der Charité*, Berlin.

|| Tardieu: *Op. Cit.*, Case 31.

ment by turpentine recovered, the blood was frequently examined, and the leucocytes found much increased in number. There is a curious conflict of evidence as to whether phosphorus prevents coagulation of the blood or not. Nasse asserted that phosphorated oil given to a dog fully prevented coagulation; P. I. Liebreck * also, in a series of researches, found the blood dark, fluid, and in perfect solution. These observations were also supported by V. Bibra and Schuchardt.† Nevertheless Lebert and Wyss found the blood, whether in the veins or in extravasations, in a normal condition. Phosphorus increases the fatty contents of the blood. Ritter found that phosphorus mixed with starch, and given to a dog, raised the fatty content from the normal 2 per thousand up to 3·41 and 3·47 per thousand. Eug. Menard ‡ saw in the blood from the jugular and portal veins, as well as in extravasations, microscopic fat globules and fine needle-shaped crystals soluble in ether.

Antidote—Treatment.—After emptying the stomach by means of emetics or by the stomach-pump, oil of turpentine in full medicinal doses, say 2·5 cc. (about 40 min.), frequently administered, seems to act as a true antidote, and a large percentage of cases treated early in this way recover.

Poisonous Effects of Phosphine (Phosphuretted hydrogen).—Experiments on pigeons, on rats, and other animals, and a few very rare cases among men, have shown that phosphine has an exciting action on the respiratory mucous membranes, and a secondary action on the nervous system. Eulenberg § exposed a pigeon to an atmosphere containing 1·68 per cent. of phosphine. There was an immediate unrest; at the end of three minutes, quickened and laboured breathing (100 a minute); after seven minutes, the bird lay prostrate, with shivering of the body and wide open beak; after eight minutes, there was vomiting; after nine minutes, slow breathing (34 per minute); after twelve minutes, convulsive movements of the wings; and after thirteen minutes, general convulsions and death.

The membranes of the brain were found strongly injected, and there were extravasations. In the mucous membrane of the crop there was also an extravasation. The lungs externally and throughout were of a dirty brown-red colour; the entire heart was filled with coagulated blood, which was weakly acid in reaction.

* *Diss. de Venefico Phosphoreo Acuto.* Upsal, 1845.

† V. Bibra u. Geist, *Die Krankheiten der Arbeiter in den Phosphorzundholz Fabriken*, 1847, S. 59, &c.—Henle u. v. Pfeuffer's *Zeitschr. f. Ration. Med.*, N. F., Bd. 7, Hft. 3, 1857.

‡ *Étude Expérimentale sur quelques lésions de l'Empoisonnement aigu par le Phosphore.* Thèse, Strasbourg, 1869.

§ *Gewerbe Hygiène*, p. 278

In a second experiment with another pigeon, there was no striking symptom save that of increased frequency of respiration and loss of appetite ; at the end of four days it was found dead. There was much congestion of the cerebral veins and vessels, the mucous membrane of the trachea and bronchia were weakly injected, and the first showed a thin, plastic, diphtheritic-like exudation.

Dr. Henderson's* researches on rats may also be noticed here. He found that an atmosphere consisting entirely of phosphine killed rats within ten minutes, an atmosphere with 1 per cent. in half an hour. The symptoms observed were almost exactly similar to those noticed in the first experiment on the pigeon quoted above, and the *post-mortem* appearances were not dissimilar. With smaller quantities of the gas, the first symptom was increased frequency of the respiration ; then the animals showed signs of suffering intense irritation of the skin, scratching and biting at it incessantly ; afterwards, they became drowsy, and assumed a very peculiar attitude, sitting down on all-fours, with the back bent forward, and the nose pushed backwards between the forepaws, so as to bring the forehead against the floor of the cage. When in this position, the rat presented the appearance of a curled-up hedge-hog. Phosphine, when injected into the rectum, is also fatal ; the animals exhale some of the gas from the lungs, and the breath, therefore, reduces solutions of silver nitrate.†

Brenner ‡ has recorded the case of a man twenty-eight years old, a pharmacist, who is supposed to have suffered from illness caused by repeated inhalations of minute quantities of phosphine. He was engaged for two and a half years in the preparation of hypophosphites ; his illness commenced with spots before the eyes and inability to fix the attention. His teeth became very brittle, and healthy as well as carious, and broke off from very slight causes. Finally, a weakness of the arms and limbs developed in the course of nine months into complete locomotor ataxy.

Blood takes up far more phosphine than water. Dybskowsky found that putting the coefficient of solubility of phosphine in pure water, at .1122 at 15°, the coefficient for venous blood was .13, and for arterial, .2673 ; hence the richer the blood is in oxygen the more phosphine is absorbed. It seems probable that the poisonous gas reacts on the oxyhaemoglobin of the blood, and phosphorus acid is formed. This is supported by the fact that a watery extract of such blood reduces silver nitrate, and has been also found feebly acid. The dark blood obtained

* *Journ. Anat. and Physiol.*, vol. xiii., p. 19.

† Dybskowsky, *Med. Chem. Untersuchungen aus Hoppe-Seyler's Labor. in Tübingen*, p. 57.

‡ *St. Petersberg Med. Zeitschr.*, 4 Hft., 1865.

from animals poisoned by phosphine, when examined spectroscopically, has been found to exhibit a band in the violet.

Post-mortem Appearances.—There are a few perfectly well authenticated cases showing that phosphorus may cause death, and yet no lesion be discovered afterwards. Thus, Tardieu* cites a case in which a woman, aged forty-five, poisoned herself with phosphorus, and died suddenly the seventh day afterwards. Dr. Mascarel examined the viscera with the greatest care, but could discover absolutely no abnormal condition; the only symptoms during life were vomiting, and afterwards a little indigestion. It may however, be remarked that the microscope does not seem to have been employed, and that probably a close examination of the heart would have revealed some alteration of its ultimate structure. The case quoted by Taylor† may also be mentioned, in which a child was caught in the act of sucking phosphorus matches, and died ten days afterwards in convulsions. None of the ordinary *post-mortem* signs of poisoning by phosphorus were met with, but the intestines were reddened throughout, and there were no less than ten invaginations; but the case is altogether a doubtful one, and no phosphorus may actually have been taken. It is very difficult to give in a limited space anything like a full picture of the different lesions found after death from phosphorus, for they vary according as to whether the death is speedy or prolonged, whether the phosphorus has been taken as a finely-divided solid, or in the form of vapour, &c. It may, however, be shortly said, that the most common changes are fatty infiltration of the liver and kidneys, fatty degeneration of the heart, enlargement of the liver, ecchymoses in the serous membranes, in the muscular, in the fatty, and in the mucous tissues. When death occurs before jaundice supervenes, there may be little in the aspect of the corpse to raise a suspicion of poison; but if intense jaundice has existed during life, the yellow staining of the skin, and it may be, spots of purpura, will suggest to the experienced pathologist, the possibility of phosphorus poisoning. In the mouth and throat there will seldom be anything abnormal. In one or two cases of rapid death among infants, some traces of the matches which had been sucked were found clinging to the gums. The stomach may be healthy, but the most common appearance is a swelling of the mucous membrane and superficial erosions. Virchow,‡ who was the first to call attention to this peculiar gray swelling of the intestinal mucous membrane under the name of *gastritis glandularis* or *gastradenitis*, shows that it is due to a fatty degeneration of the epithelial cells,

* *L'Empoisonnement*, p. 520.

† "Poisons," 3rd Ed., p. 276.

‡ *Virchow's Archiv f. Path. Anat.*, Bd. 31, Hft. 3., 399, S. 1864.

and that it is by no means peculiar to phosphorus poisoning. The swelling may be seen by properly-prepared sections to have its essential seat in the glands of the mucous membrane ; the glands are enlarged, their openings filled with large cells, and each single cell is finely granular. Little centres of haemorrhage, often microscopically small, are seen, and may be the centres of small inflammations ; their usual situation is on the summit of the rugæ. Very similar changes are witnessed after death from septicæmia, pyæmia, diphtheria, and other diseases. The softening of the stomach, gangrene, and deep erosions, recorded by the earlier authors, have not been observed of late years, and probably were due to *post-mortem* changes, and not to processes during life. The same changes are to be seen in the intestines, and there are numerous extravasations in the peritoneum.

The liver shows of all the organs the most characteristic signs ; a more or less advanced fatty infiltration of its structure takes place, which was first described as caused by phosphorus by Hauff in 1860.* It is the most constant pathological evidence both in man and animal, and seems to occur at a very early period, Munk and Leyden having found a fatty degeneration in the liver far advanced in twenty-four hours† after poisoning. In rats and mice poisoned with paste, I have found the processes evident to the naked eye twelve hours after the fatal dose. The liver is mostly large ; has a pale yellow (or sometimes an intense yellow) colour ; on section the cut surface presents a mottled appearance ; the serous envelopes, especially along the course of the vessels, exhibit extravasations of blood. The liver itself is more deficient in blood than in the normal condition, and the more bloodless it is, the greater the fatty infiltration.

The microscopic appearances are also characteristic. In a recent case of suicidal poisoning by phosphorus, in which death took place on the seventh day, the liver was very carefully examined by Dr. G. F. Goodart, who reports as follows :—

"Under a low power the structure of the liver is still readily recognisable, and in this the specimen differs from slides of three cases of acute yellow atrophy that I have in my possession. The hepatic cells are present in large numbers, and have their natural trabecular arrangement. The columns are abnormally separated by dilated blood or lymph spaces, and the individual cells are cloudy and ill-defined. The portal channels are everywhere characterised by a crowd of small nuclei which stain with logwood deeply. The epithelium of the smaller ducts is cloudy, and blocks the tubes in many cases. Under a high power (one-fifth) it is seen that the hepatic cells are exceedingly ill-defined in outline, and full of granules and even drops of oil. But in many parts, even where

* Hauff collected 12 cases and found a fatty liver in 11.—*Würtemb. Med. Correspond. Bl.*, 1860, No. 34.

† *Die Acute Phosphor-Vergiftung.* Berlin, 1865.

the cells themselves are hazy, the nucleus is still fairly visible. It appears to me that, in opposition to what others have described, the nuclei of the cells have in great measure resisted the degenerative process. The change in the cells is uniform throughout each lobule, but some lobules are rather more affected than others. The blood spaces between the cells are empty, and the liver appears to be very bloodless. The portal canals are uniformly studded with small round nuclei or cells, which are in part, and might be said in great part, due to increase of the connective tissue or to a cirrhotic process. But I am more disposed to favour the view that they are due to migration from the blood-vessels, because they are so uniform in size, and the hepatic cells and connective tissue in their neighbourhood are undergoing no changes in the way of growth whatever. I cannot detect any fatty changes in the vessels, but some of the smaller biliary ducts contain some cloudy albuminous material, and their nucleation is not distinct. No retained biliary pigment is visible."*

Oscar Wyss,† in the case of a woman twenty-three years old, who died on the fifth day after taking phosphorus, describes, in addition to the fatty appearance of the cells, a new formation of cells lying between the lobules and in part surrounding the gall-ducts and the branches of the portal vein and hepatic artery.

Saikowsky ‡ found in animals, which he killed a few hours after administering to them toxic doses of phosphorus, notable hyperæmia of the throat, intestine, liver, and kidneys—both the latter organs being larger than usual. The liver cells were swollen, and the nuclei very evident, but they contained no fat, fatty drops being formed afterwards.

The Kidneys exhibit alterations very similar and analogous to those of the liver. They are mostly enlarged, congested, and flabby, with extravasations under the capsule, and show microscopic changes essentially consisting in a fatty degeneration of the epithelium. In cases attended with haemorrhage, the tubuli may be here and there filled with blood. The fatty epithelium is especially seen in the contorted tubes, and the walls of the vessels, both of the capsule and of the malpighian bodies, also undergo the same fatty change. In cases in which death has occurred rapidly, the kidneys have been found almost healthy or a little congested only. The pancreas has also been found with its structure in part replaced by fatty elements.

Of great significance are also the fatty changes in the general muscular system, and more especially in the heart. The muscular fibres of the heart quickly lose their transverse striae, which are replaced by drops of fat. Probably this change is the cause of the sudden death not unfrequently met with in phosphorus poisoning.

* "A Recent Case of Suicide," By Herbert J. Capon, M.D.—*Lancet*, March 18, 1882.

† *Virchow's Archiv f. Path. Anat.*, Bd. 33, Hft. 3, S. 432, 1865.

‡ *Ibid.*, Bd. 34, Hft. 1 u. 2, S. 73, 1865.

In the Lungs, when the phosphorus is taken in substance, there is little "naked-eye" change, but Perls,* by manometric researches, has shown that the elasticity is always decreased. According to experiments on animals, when the vapour is breathed, the mucous membrane is red, congested, swollen, and has an acid reaction.

In the Nervous System no change has been remarked, save occasionally haemorrhagic points and extravasations.

Diagnostic Differences between Acute Yellow Atrophy of the Liver and Fatty Liver produced by Phosphorus.—O. Schultzen and O. L. Riess have collected and compared ten cases of fatty liver from phosphorus poisoning, and four cases of acute yellow atrophy of the liver, and, according to them, the chief points of distinction are as follows:—In phosphorus poisoning the liver is large, doughy, equally yellow, and with the acini well marked; while in acute yellow atrophy the liver is diminished in size, tough, leathery, and of a dirty yellow hue, the acini not being well mapped out. The "phosphorus" liver, again, presents the cells filled with large fat drops, or entirely replaced by them; but in the "atrophy" liver, the cells are replaced by a finely-nucleated detritus and through newly-formed cellular tissue. Yellow atrophy seems to be essentially an inflammation of the intralobular connective tissue, while in phosphorus poisoning the cells become gorged by an infiltration of fat, which presses upon the vessels and lessens the blood supply, and the liver, in consequence, may, after a time, waste.

There is also a clinical distinction during life, not only in the lessening bulk of the liver in yellow atrophy, in opposition to the increase of size in the large phosphorus liver, but also in the composition of the renal secretion. In yellow atrophy the urine contains so much leucine and tyrosin, that the simple addition of acetic acid causes at once a precipitate. Scultzen and Riess also found in the urine, in cases of yellow atrophy, *oxymandelic acid* ($C_8H_8O_4$), but in cases of phosphorus poisoning a nitrogenised acid, fusing at 184° to 185° .

According to Maschka, gray-white, knotty, faecal masses are found in the intestines in yellow atrophy, but never in cases of phosphorus poisoning. In the latter it is more common to find a slight intestinal catarrh and fluid excreta.

The Detection of Phosphorus.—The following are the chief methods in use for the separation and detection of phosphorus:—†

* *Deutsch. Archiv f. Klin. Med.*, vi., Hft. 1, S. 1, 1869.

† It has been recommended to dissolve the phosphorus out from organic matters by carbonic disulphide. On evaporation of the latter, the phosphorus is recognised by its physical properties. Such a method is of but limited application, although it may sometimes be found useful. I have successfully employed it in the extraction of phosphorus from the crop of a fowl; but on this occasion it happened to be present in large quantity.

1. *Mitscherlich's Process.*—The essential feature of this process is simply distillation of free phosphorus, and observation of its luminous properties as the vapour condenses in the condensing tube. The conditions necessary for success are—(1) that the apparatus should be in total darkness ; * and (2) that there should be no substance present, such as alcohol or ammonia,† which, distilling over with the phosphorus-vapour, could destroy its luminosity. A convenient apparatus, and one certain to be in all laboratories, is an ordinary Florence flask, containing the liquid to be tested, fitted to a glass Liebig's condenser, supported on an iron sand-bath, which may, or may not, have a thin layer of sand), and heated by a Fletcher's low temperature burner. The distillate is received into a flask. This apparatus, if in darkness, works well ; but should the observer wish to work in daylight, the condenser must be enclosed in a box perfectly impervious to light, and having a hole through which the luminosity of the tube may be seen, the head of the operator and the box being covered with a cloth. If there be a stream of water passing continuously through the condenser, a beautiful luminous ring of light appears in the upper part of the tube, where it remains fixed for some time. Should, however, the refrigeration be imperfect, the luminosity travels slowly down the tube into the receiver. In any case, the delicacy of the test is extraordinary.‡ If the organic liquid is alkaline, or even neutral, there will certainly be some evolution of ammonia, which will distil over before the phosphorus, and retard (or, if in sufficient quantity, destroy) the luminosity. In such a case it is well, as a precaution, to add enough sulphuric acid to fix the ammonia, omitting such addition if the liquid to be operated upon is acid.

2. *The Production of Phosphine (PH₃).*—Any method which produces phosphine (phosphuretted hydrogen), enabling that gas to be passed through nitrate of silver solution, may be used for the detection of phosphorus. Thus Sonnenschein states that he has found phosphorus in extraordinarily small amount, mixed with various substances, by heating with potash in a flask, and passing the phosphine into silver nitrate, separating the excess of silver, and recognising the phosphoric acid by the addition of molybdate of ammonia.§

* Any considerable amount of phosphorescence can, however, be observed in twilight.

† A variety of volatile substances destroys the luminous appearance of phosphorus vapour—*e. g.*, chlorine, hydric sulphide, sulphur dioxide, carbon disulphide, ether, alcohol, petroleum, turpentine, creasote, and most essential oils. On the other hand, bromine, hydrochloric acid, camphor, and carbonate of ammonia do not seem to interfere much with the phosphorescence.

‡ Fresenius states that he and Neubauer, with 1 mgrm. of phosphorus in 200,000, recognised the light, which lasted for half an hour.—*Zeitsch. f. Anal. Chem.*, i., p. 336.

§ Sonnenschein, *Handbuch der Gerichtlichen Chemie*. Berlin, 1869.

3. *Tests Dependent on the Combustion of Phosphine (PH₃).*—A hydrogen flame, containing only a minute trace of phosphorus, or of the lower products of its oxidation, acquires a beautiful green tint, and possesses a characteristic *spectrum*. In order to obtain the latter in its best form, the amount of phosphine must not be too large, or the flame will become whitish and livid, and the bands lose their defined character, rendering the spectrum continuous. Again, the orifice of the tube, whence the gas escapes, must not be too small ; and the best result is obtained when the flame is cooled.

M. Salet has proposed two excellent methods for the observation of phosphine by the spectroscope :—

(1.) He projects the phosphorus-flame on a plane vertical surface, maintained constantly cold by means of a thin layer of running water ; the green colour is especially produced in the neighborhood of the cool surface.

(2.) At the level of the base of the flame, there is an annular space, through which a stream of cold air is continually blown upwards. Thus cooled, the light is very pronounced, and the band, δ , which is almost invisible in the ordinary method of examination, is plainly seen.*

An apparatus (devised by Blondlot, and improved by Fresenius), for the production of the phosphine flame in medico-legal research, is represented in the following diagram :—

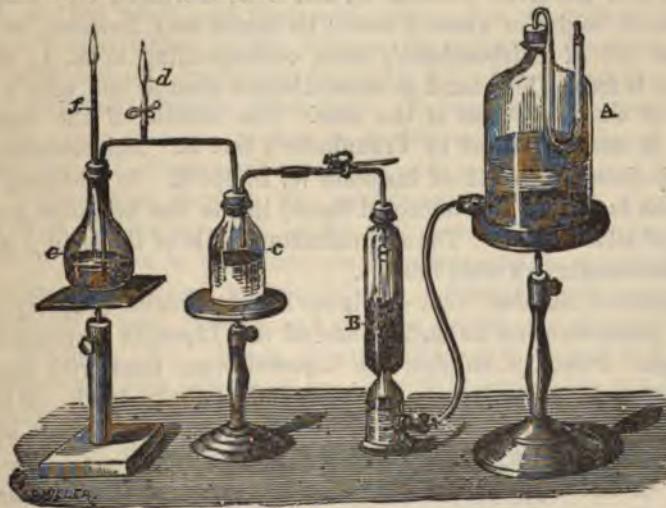


Fig. 12

* Consult *Spectres Lumineux* par M. Lecoq de Boisbaudran. Paris, 1874. See also Christofle and Beilstrom's *Abhandlung* in *Fresenius' Zeitschr. f. Anal. Chem.*, B. 2, p. 465, and B. 3, p. 147.

Several of the details of this apparatus may be modified at the convenience of the operator. A is a vessel containing sulphuric acid ; B is partly filled with granulated zinc, and hydrogen may be developed at pleasure ; c contains a solution of nitrate of silver ; d is a tube at which the gas can be lit ; e, a flask containing the fluid to be tested, and provided with a tube f, at which also the gas issuing can be ignited. The orifice should be provided with a platinum nozzle. When the hydrogen has displaced the air, both tubes are lit, and the two flames, being side by side, can be compared. Should any phosphorus come over from the zinc (a possibility which the interposed silver nitrate ought to guard against), it is detected ; the last flask is now gently warmed, and if the flame is green, or indeed, in any case, it should be examined by the spectroscope.*

The spectrum, when fully developed, shows one band in the orange and yellow between C and D, but very close to D, and several bands in the green. But the bands, δ γ α , and β , are the most characteristic. The band δ has its centre about the wave-length 599.4 ; it is easily distinguished when the slit of the spectroscope is a little wide, but may be invisible if the slit is too narrow. It is best seen by M. Salet's second process, and, when cooled by a brisk current of air, it broadens, and may extend closer to D. The band γ has a somewhat decided border towards E, while it is nebulous towards D, and it is, therefore, very difficult to say where it begins or where it ends ; its centre may, however, be put at very near 109 of Boisbeaubran's scale, corresponding to W. L. 560.5, if the flame is free. This band is more distinct than β , but with a strong current of air the reverse is the case. The middle of the important band α is nearly marked by Fraunhofer's line E. Boisbeaubran gives it as coinciding with 122 of his scale W. L. 526.3. In ordinary conditions (that is, with a free uncooled flame) this is the brightest and most marked of all the bands. The approximate middle of the band β is W. L. 510.6 (Boisbeaubran's scale 129.00).

Lipowitz's Sulphur Test.—Sulphur has the peculiar property of condensing phosphorus on its surface, and of this Lipowitz proposed to take advantage. Pieces of sulphur are digested some time with the liquid under research, subsequently removed, and slightly dried. When examined in the dark, should phosphorus be present, they gleam strongly if rubbed with the finger, and develop a phosphorus odour. The test is wanting in delicacy, nor can it well be made quantitative ; it has, however, an advantage in certain cases—*e.g.*, the detection of phosphorus in alcoholic liquid.

* F. Selmi has proposed the simple dipping of a platinum loop into a liquid containing phosphoric acid, and then inserting it into the tip of a hydrogen flame.

Scherer's test, as modified by Hager,* is a very delicate and almost decisive test. The substances to be examined are placed in a flask with a little lead acetate (to prevent the possibility of any hydric sulphide being evolved), some ether added, and a strip of filter paper soaked in a solution of silver nitrate is then suspended in the flask ; this is conveniently done by making a slit in the bottom of the cork, and in the slit securing the paper. The closed flask is placed in the dark, and if phosphorus is present, in a few minutes there is a black stain. It may be objected that arsine will cause a similar staining, but then arsine could hardly be developed under the circumstances given. It is scarcely necessary to observe that the paper must be wet.

Chemical Examination of the Urine.—It may be desirable, in any case of suspected phosphorus poisoning, to examine the renal secretion for leucin and tyrosin, &c. Leucin may be found as a deposit in the urine. Its general appearance is that of little oval or round discs, looking like drops of fat. It can be recognised by taking up one or more of these little bodies and placing them in the author's subliming cell (see Index). By careful heating it will sublime wholly on to the upper cover. On now adding a little nitric acid to the sublimed leucin, and drying, and then to the dried residue adding a droplet of a solution of sodium hydrate, leucin forms an oily drop. Tyrosin also may occur as a sediment of little heaps of fine needles. The best test for tyrosin is to dissolve in hot water, and then add a drop of a solution of mercuric nitrate and mercurous nitrate, when a rose colour is at once developed, if the tyrosin is in very minute quantity, but if in more than traces, there is a distinct crimson precipitate. To separate leucin and tyrosin from the urine, the best process is as follows :—The urine is filtered from any deposit, evaporated to a thin syrup, and decanted from the second deposit that forms. The two deposits are mixed together and treated with dilute ammonia, which will dissolve out any tyrosin and leave it in needles, if the ammonia is spontaneously evaporated on a watch glass. The urine is then diluted and treated with neutral and basic acetates of lead, filtered, and the lead thrown out of the filtrate by hydric sulphide. The filtrate is evaporated to a syrup, and it then deposits leucin mixed with some tyrosin. If, however, the syrup refuses to crystallise, it is treated with cold absolute alcohol, and filtered, the residue is then boiled up with spirit of wine, which extracts leucin, and deposits it on cooling in a crystalline form. To obtain oxy-mandelic acid, the mother liquor, from which leucin and tyrosin have been extracted, is precipitated with absolute alcohol, filtered, and then the alcoholic solution evaporated to a syrup. This syrup is acidified by sulphuric acid, and extracted with ether ; the ether is filtered off and

* *Pharm. Central-halle*, 20, 353.

evaporated to dryness; the dry residue will be in the form of oily drops and crystals. The crystals are collected, dissolved in water, and the solution precipitated by lead acetate to remove coloring-matters; after filtration it is finally precipitated by basic acetate. On decomposition of the basic acetate, by suspending in water and saturating with hydric sulphide, the ultimate filtrate on evaporation deposits colourless flexible needles of oxymandelic acid. The nitrogenised acid which Schultzen and Riess obtained from urine in a case of phosphorus poisoning, was found in an alcohol and ether extract—warts of rhombic scales separating out of the syrupy residue. These scales gave no precipitate with basic acetate, but formed a compound with silver nitrate. The silver compound was in the form of shining white needles, and contained 33.9 per cent. of silver; the acid was decomposed by heat, and with lime yielded aniline. Its melting point is given at from 184° to 185°. The occurrence of some volatile substance in phosphorus urine, which blackens nitrate of silver, and which is probably phosphine, was first noticed by Selmi.* Pesci and Stroppa have confirmed Selmi's researches. It is even given off in the cold.

The Quantitative Estimation of Phosphorus is best carried out by oxidising it into phosphoric acid, and estimating as ammon. magnesian phosphate. To effect this, the substances are distilled in an atmosphere of CO_2 into a flask with water, to which a tube containing silver nitrate is attached; the latter retains all phosphine, the former solid phosphorus. If necessary, the distillate may be again distilled into AgNO_3 ; and in any case the contents of the **U** tube and flask are mixed, oxidised with nitromuriatic acid, filtered from silver chloride, and the phosphoric acid determined in the usual way.

In the case of a child poisoned by lucifer matches, Sonnenschein estimated the free phosphorus in the following way:—The contents of the stomach were diluted with water, a measured part filtered, and the phosphoric acid estimated. The other portion was then oxidised by HCl and potassic chlorate, and the phosphoric acid estimated—the difference being calculated as free phosphorus.

How long can Phosphorus be recognised after Death?—One of the most important matters for consideration is the time after death in which free phosphorus, or free phosphoric acids, can be detected. Any phosphorus changed into ammon. mag. phosphate, or into any other salt, is for medico-legal purposes entirely lost, since the expert can only take cognisance of the substance either in a free state, as phosphine, or as a free acid.

The question again, may be asked in court—Does the decomposition

**Giornale Internaz. della Scienza Med.*, 1879, Nro. 5, p. 645.

of animal substances rich in phosphorus developed phosphine? The answer to this is, that no such reaction has been observed.

A case is related* in which phosphorus was recognised, although the body had been buried for several weeks, and then exhumed.

The expert of pharmacy of the Provincial Government Board of Breslau has also made some experiments in this direction, which are worthy of note:—Four guinea pigs were poisoned, each by 0.023 grm. of phosphorus; they died in a few hours, and were buried in sandy-loam soil, 0.5 metre deep. Exhumation of the first took place four weeks after. The putrefying organs—heart, liver, spleen, stomach, and all the intestines, tested by Mitscherlich's method of distillation, showed characteristic phosphorescence for nearly an hour.

The second animal was exhumed after eight weeks in a highly putrescent state. Its entrails, on distillation, showed the phosphorescent appearance for thirty-five minutes.

The third animal was taken from the earth after twelve weeks, but no free phosphorus could be detected, although there was evidence of the lower form of oxidation (PO_3) by Blondlot's method.

The fourth animal was exhumed after fifteen weeks, but neither free phosphorus nor PO_3 could be detected.†

A man, as well as a cat, was poisoned by phosphorus. On analysis, twenty-nine days after death, negative results were alone obtained. (*Sonnenschein*).

It will thus be evident that there is no constant rule, and that, even when decomposition is much advanced, an examination *may* be successful.

* *Pharm. Zeitsch. f. Russl.* ; Jahrg. 2, p. 87.

† *Vierteljahrsschrift für Gerichtliche Medicin*, Jan. 7, 1876.—See also *Zeitschr. f. Anal. Chemie*, 1872.

PART V.—ALKALOIDS AND POISONOUS VEGETABLE PRINCIPLES SEPARATED FOR THE MOST PART BY ALCOHOLIC SOLVENTS.

DIVISION I.—VEGETABLE ALKALOIDS.

1. GENERAL METHOD OF TESTING AND EXTRACTING ALKALOIDS.

General Tests for Alkaloids.—In order to ascertain whether an alkaloid is present or not, a method of extraction must be pursued which, while disposing of fatty matters, salts, &c., shall dissolve as little as possible of foreign substances; such a method, *e.g.*, as the original process of Stas, or one of its modern modifications.

If to the acid aqueous solution finally obtained by this method a dilute solution of soda be added, drop by drop until it is rendered feebly alkaline, *and no precipitate appear*, whatever other poisonous plant-constituents may be present, all ordinary alkaloids * are absent.

In addition to this negative test, there are also a number of substances which give well-marked crystalline or amorphous precipitates with alkaloids.

These may be called “group-reagents.” The chief members of the group-reagents are—iodine dissolved in hydriodic acid, iodine dissolved in potassic iodide solution, bromine dissolved in potassic bromine solution, hydrargo-potassic iodide, bismuth-potassic iodide, cadmic potassic iodide; the chlorides of gold, of platinum, and mercury; picric acid, gallic acid, tannin, chromate of potash, bichromate of potash, phosphomolybdic acid, phospho-tungstic acid, silico-tungstic acid, and Fröhde’s reagents. It will be useful to make a few general remarks on some of these reagents.

Iodine in Hydriodic Acid gives either crystalline or amorphous precipitates with nearly all alkaloids; the compound with morphine, for example, is in very definite needles; with dilute solutions of atropine, the

* In the case of morphine tartrate, this test will not answer. See the article on morphine.

precipitate is in the form of minute dots, but the majority of the precipitates are amorphous, and all are more or less coloured.

Iodine Dissolved in a Solution of Potassic Iodide gives with alkaloids a reddish or red-brown precipitate, and this in perhaps a greater dilution than almost any reagent. When added to an aqueous solution, the precipitates are amorphous, but if added to an alcoholic solution, certain alkaloids then form crystalline precipitates ; this, for example, is the case with berberine and narceine. By treating the precipitate with aqueous sulphurous acid, a sulphate of the alkaloid is formed and hydriodic acid, so that by suitable operations the alkaloid may readily be recovered from this compound. A solution of bromine in potassic bromide solution also gives similar precipitates to the above, but it forms insoluble compounds with phenol, orcin, and other substances.

Mercuric Potassic Iodide is prepared by decomposing mercuric chloride with potassic iodide in excess. The proportions are 13·546 grms. of mercuric chloride and 49·8 of potassic iodide, and water sufficient to measure, when dissolved, one litre. The precipitates from this reagent are white and flocculent ; many of them become, on standing, crystalline.

Bismuthic Potassic Iodide in solution precipitates alkaloids, and the compounds formed are of great insolubility, but it also forms compounds with the various albuminoid bodies.

Chloride of Gold forms with the alkaloids compounds, many of which are crystalline, and most admit of utilisation for quantitative determinations. Chloride of gold does not precipitate amides or ammonium compounds, and on this account its value is great. The precipitates are yellow, and after a while are partly decomposed, when the colour is of a reddish-brown.

Platinic Chloride also forms precipitates with most of the alkaloids, but since it also precipitates ammonia and potassic salts, it is inferior to gold chloride in utility.

(1) *Phosphomolybdic Acid as a Reagent for Alkaloids.*—*Preparation* : Molybdate of ammonia is precipitated by phosphate of soda ; and the well-washed yellow precipitate is suspended in water and warmed with carbonate of soda, until it is entirely dissolved. This solution is evaporated to dryness, and the ammonia fully expelled by heating. If the molybdic acid is fairly reduced by this means, it is to be moistened by nitric acid, and the heating repeated. The now dry residue is warmed with water, nitric acid added to strong acid reaction, and the mixture diluted with water, so that 10 parts of the solution contain 1 of the dry salt. The precipitates of the alkaloids are as follows :—

Aniline,	Bright-yellow, flocculent.
Morphine,	" " "

Narcotine,	Brownish-yellow, flocculent,
Quinine,	Whitish-yellow, "
Cinchonine,	"
Codeine,	Brownish-yellow, voluminous,
Strychnine,	White-yellow, "
Brucine,	Yelk yellow, flocculent,
Veratrine,	Bright-yellow, "
Jervine,	" "
Aconitine,	" "
Emetine,	" "
Theine,	Bright-yellow, voluminous,
Theobromine,	" "
Solanine,	Citron-yellow, pulverulent,
Atropine,	Bright-yellow, flocculent,
Hyoscyamine,	" "
Colchicine,	Orange-yellow, "
Delphinine,	Gray-yellow, voluminous,
Berberine,	Dirty-yellow, flocculent,
Coniine,	Bright-yellow, voluminous,
Nicotine,	" "
Piperine,	Brownish-yellow, flocculent.

(2.) *Silico-Tungstic Acid as a Reagent for Alkaloids.*—Sodium tungstate is boiled with freshly precipitated gelatinous silica. To the solution is added mercurous nitrate, which precipitates the yellow mercurous silico-tungstate. This is filtered, well washed, and decomposed by an equivalent quantity of hydrochloric acid; silico-tungstic acid then goes into solution, and mercurous chloride (calomel) remains behind. The clear filtrate is evaporated to drive off the excess of hydrochloric acid, and furnishes, on spontaneous evaporation, large, shining, colourless octahedra of silico-tungstic acid, which effloresce in the air, melt at 36°, and are easily soluble in water or alcohol.

This agent produces no insoluble precipitate with any metallic salt. Cœsium and rubidium salts, even in dilute solutions are precipitated by it; neutral solutions of ammonium chloride give with it a white-precipitate, soluble with difficulty in large quantities of water. It precipitates solutions of the salts of quinine, cinchonine, morphine, atropine, &c.; if in extremely dilute solution, an opalescence only is produced; for instance, it has been observed that cinchonine hydrochlorate in $\frac{1}{30000}$, quinia hydrochlorate in $\frac{1}{30000}$, morphia hydrochlorate in $\frac{1}{1225}$ dilution, all gave a distinct opalescence. (*Archiv der Pharm.*, Nov., Dr. Richard Godeffroy).

(3.) *Schiebler's Method for Alkaloids: Phospho-Tungstic Acid.*—Ordinary commercial sodium tungstate is digested with half its weight of phosphoric acid, specific gravity 1.13, and the whole allowed to stand for some days, when the acid separates in crystals. A solution of these crystals will give a distinct precipitate with the most minute quantities

of alkaloids, $\frac{1}{20000}$ of strychnine, and $\frac{1}{10000}$ of quinine. The alkaloid is liberated by digestion with barium hydrate (or calcium hydrate); and if volatile, may be distilled off; if fixed, dissolved out by chloroform. In complex mixtures, colouring-matter may be removed by plumbic acetate, the lead thrown out by SH_2 , and concentrated, so as to remove the excess of SH_2 .

Fröhde's Reagent.—This is a colour reagent, and is made by dissolving 1 part of sodic molybdate in 10 parts of strong sulphuric acid.

Stas's Process.—The original method of Stas* (afterwards modified by Otto),† consisted in extraction of the organic matters by strong alcohol, with the addition of tartaric acid; the filtered solution was then carefully neutralised with soda, and shaken up with ether, the ethereal solution being separated by a pipette. Subsequent chemists proposed chloroform instead of ether,‡ the additional use of amyl-alcohol,§ and the substitution of acetic, hydrochloric, and sulphuric for tartaric acid.

METHODS OF SEPARATION.

Selmi's Process for Separating Alkaloids.—A method of separating alkaloids from an ethereal solution has been recently proposed by Selmi.|| The alcoholic extract of the viscera, acidified and filtered, is evaporated at 65° ; the residue taken up with water, filtered, and decolorised by basic acetate of lead. The lead is thrown out by sulphuretted hydrogen; the solution, after concentration, repeatedly extracted with ether; and the ethereal solution saturated with dry CO_2 , which generally precipitates some of the alkaloids. The ethereal solution is then poured into a clean vessel, and mixed with about half its volume of water, through which a current of CO_2 is passed for 20 minutes; this may cause the precipitation of other alkaloids not thrown down by dry CO_2 . If the whole of the alkaloids are not obtained by these means, the solution is dehydrated by agitation with barium oxide, and a solution of tartaric acid in ether is added (care being taken to avoid excess); this throws down any alkaloid still present. The detection of any yet remaining in the viscera is effected by mixing with barium hydrate and a little water, and agitating with purified amylic alcohol; from the alcohol the alkaloids may be subsequently extracted by agitation with very dilute sulphuric acid.

* *Annal. d. Chem. u. Pharm.*, 84, 379.

† *Ib.* 100, 44. *Anleitung zur Ausmittel. d. Gifte*.

‡ Rodgers and Girwood. *Pharm. Journ. and Trans.*, 16, 497; Prollin's *Chem. Centralb.*, 1857, 231; Thomas, *Zeitschr. fur Analyt. Chem.*, i., 517, &c.

§ Erdmann and v. Ushlar, *Ann. Chem. Pharm.*, cxx., pp. 121-360.

|| F. Selmi, *Gazett. Chim. Ital.*, vj. 153-166, and *Journ. Chem. Soc.*, i., 1877, 93.

Another ingenious method (also the suggestion of Selmi) is to treat the organic substance with alcohol, to which a little sulphuric acid has been added, to filter, digest with alcohol and refilter. The filtrates are united, evaporated down to a smaller bulk, filtered, concentrated to a syrup, alkalised by barium hydrate, and after the addition of freshly ignited barium oxide and some powdered glass, exhausted with dry ether; the ether filtered, the filtrate digested with lead hydrate; the ethereal solution filtered, evaporated to dryness, and finally again taken up with ether, which, this time, should leave on evaporation the alkaloid almost pure.

Dragendorff's Process.—To Dragendorff we owe an elaborate general method of separation, since it is applicable, not only to alkaloids, but to glucosides, and other active principles derived from plants. His process is essentially a combination of those already known, and its distinctive features are the shaking up—(1) of the acid fluid with the solvent, thus removing colouring-matters and certain non-alkaloidal principles; and (2) of the same fluid made alkaline. The following is his method in full. It may be advantageously used when the analyst has to search generally for vegetable poison, although it is, of course, far too elaborate for every case; and where from any circumstance there is good ground for suspecting the presence of one or two particular alkaloids or poisons, the process may be much shortened and modified.*

I. The substance, in as finely-divided form as possible, is digested for a few hours in water acidified with sulphuric acid, at a temperature of 40° to 50° , and this operation is repeated two or three times, with filtering and pressing of the substances; later, the extracts are united. This treatment (if the temperature mentioned is not exceeded) does not decompose the majority of alkaloids or other active substances; but there are a few (*e. g.*, solanine and colchicine) which would be altered by it; and if such are suspected, maceration at the common temperature is necessary, with substitution of acetic for sulphuric acid.*

II. The extract is next evaporated until it begins to be of a syrupy consistence; the residue mixed with three to four times its volume of alcohol, macerated for twenty-four hours, at about 34° , allowed to become quite cool, and filtered from the foreign matters which have separated. The residue is washed with alcohol of 70 per cent.

III. The filtrate is freed from alcohol by distillation, the watery resi-

* Dragendorff's *Gerichtlich-chemische Ermittlung von Giften*, St Petersburg, 1876, p. 141.

† When blood is to be examined it is better to dry it, and then powder and extract with water acidified with dilute sulphuric acid. However, if the so-called volatile alkaloids are suspected, this modification is to be omitted.

due poured into a capacious flask, diluted (if necessary) with water, and filtered. Acid as it is, it is extracted at the common temperature, with frequent shaking, by freshly rectified petroleum ether; and after the fluids have again separated, the petroleum ether is removed, carrying with it certain impurities (colouring matter, &c.), which are in this way advantageously displaced. By this operation ethereal oils, carbolic acid, picric acid, &c., which have not been distilled, besides piperin, may also be separated. The shaking up with petroleum ether is repeated several times (as long as anything remains to be dissolved), and the products are evaporated on several watch-glasses.

RESIDUE OF PETROLEUM ETHER FROM THE ACID
SOLUTION.

1. IT IS CRYSTAL-
LINE.

2. IT IS AMORPHOUS.

3. IT IS VOLATILE,
with a powerful
odour: *ethereal oil,*
carbolic acid, &c.

A. *It is yellowish,*
and with difficulty
volatilised.

α . The crystals are
dissolved by concen-
trated sulphuric acid,
with the production
of a clear yellow col-
our, passing into
brown and greenish-
brown.

Piperin.

β . The solution in sulphuric
acid remains yellow; potassic cy-
anide and caustic potash colour it,
on warming blood-red.

Picric acid.

B. IT IS COLOURLESS, LIQUIFIES
EASILY, AND SMELLS STRONGLY.

Camphor and similar matters.

A. It is fixed.

α . Concentrated
sulphuric acid dis-
solves it immediately
—violet, and later
greenish-blue.

*Constituents of the
black hellebore.*

β . It dissolves with a yellow col-
our, changing into fallow-brown.

*Constituents of aconite plant and
products of the decomposition
of Aconitine.*

B. IT IS WHITE, SHARP-TASTING,
AND REDDENS THE SKIN.

Capsicin.

It may be expected that the substances mentioned under the heads

1, 2, and 3, will be, in general, fully obtained by degrees. This is not the case, however, as regards piperin and picric acid.

IV. The watery fluid is now similarly shaken up with benzene, and the benzene removed and evaporated. Should the evaporated residue show signs of an alkaloid (and especially of theine), the watery fluid is treated several times with a fresh mixture of benzene, till a little of the last-obtained benzene-extraction leaves on evaporation no residue. The benzene extracts are now united, and washed by shaking with distilled water; again separated and filtered, the greater part of the benzene distilled from the filtrate, and the remainder of the fluid divided and evaporated on several watch-glasses.

The evaporated residue may contain theine, colchicine, cubebin, digitalin, cantharidin, colocynthin, elaterin, caryophylline, absinthin, cascarillin, populin, santonin, &c., and traces of veratrine, delphinine, physostigmine, and berberine.

A remnant of piperin and picric acid may remain from the previous treatment with petroleum ether.

THE BENZENE RESIDUE FROM THE ACID SOLUTION.

1. IT IS CRYSTALLINE.

A. WELL-FORMED, COLOURLESS CRYSTALS.

a. Sulphuric acid dissolves the hair-like crystals without change of colour; evaporation with chlorine water, and subsequent treatment with ammonia, gives a murioxide reaction.

Theine.

β. Sulphuric acid leaves the rhombic crystals uncoloured. The substance, taken up by oil, and applied to the skin, produces a blister.

Canthardin.

γ. Sulphuric acid leaves the scaly crystals at first uncoloured, then slowly develops a reddening. It does not blister. Warm alcoholic potash-lye colours it a transitory red.

Santonin.

2. IT IS AMORPHOUS.

A. COLOURLESS OR PALE YELLOW RESIDUE.

a. Sulphuric acid dissolves it at first yellow; the solution becoming later red. Fröhde's reagent does not colour it violet.

Elaterin.

β. Sulphuric acid dissolves red; Fröhde's reagent violet-red;* tannic acid does not precipitate.

Populin.

γ. Sulphuric acid dissolves it extremely red; Fröhde's reagent* a beautiful cherry-red; tannic acid precipitates a yellowish-white.

Colocynthin.

* Fröhde's reagent is described at page 211.

δ. Sulphuric acid colours the crystals almost black, whilst it takes itself a beautiful red colour.

Cubebin.

δ. Sulphuric acid colours it gradually a beautiful red, whilst tannin does not precipitate

Constituents of the Pimento.

B. CRYSTALS PALE TO CLEAR
YELLOW.

α. *Piperin.*

B. PURE YELLOW RESIDUE.

α. Sulphuric acid dissolves it yellow; on the addition of nitric acid, this solution is green, quickly changing to blue and violet.

Colchicine.

β. Sulphuric acid dissolves with separation of a violet powder; caustic potash colours it red; sulphide of ammonia violet, and, by heating indigo-blue.

Chrysammic acid.

γ. Caustic potash dissolves it purple.

Aloetin.

C. MOSTLY UNDEFINED COLOUR-
LESS CRYSTALS.

C. A GREENISH BITTER RESI-
DUE, which dissolves brown in concentrated sulphuric acid; in Fröhde's reagent, likewise, at first brown, then at the edge green, changing into blue-violet, and lastly violet.

Constituents of wormwood, with absynthin, besides quassiin, menyanthin, ericolin, daphnin, cnicin, and others.

α. Sulphuric acid dissolves it green brown; bromine colours this solution red; dilution with water again green. The substance renders the heart-action of a frog slower.

Digitalin.

β. Sulphuric acid dissolves it orange, then brown, lastly red-violet. Nitric acid dissolves it yellow, and water separates as a jelly out of the latter solution.

Sulphuric acid and bromine do not colour it red. *Gratiolin.*

γ. Sulphuric acid dissolves it red-brown. Bromine produces in this solution red-violet stripes. It does not act on frogs. *Cascarillin.*

D. GENERALLY UNDEFINED YELLOW CRYSTALLISATION.—Sulphuric acid dissolves it olive green. The alcoholic solution gives with potassic iodide a colourless and green crystalline precipitate. *Berberin.*

V. As a complete exhaustion of the watery solution is not yet attained by the benzene agency, another solvent is tried.

THE WATERY SOLUTION IS NOW EXTRACTED IN THE SAME WAY BY CHLOROFORM.

In chloroform the following substances are especially taken up:—Theobromine, narceine, papaverine, cinchonine, jervine, besides picrotoxin, syringin, digitalin, helleborin, convallamarin, saponin, senegin, smilacin. Lastly, portions of the bodies named in Process IV., which benzene failed to extract entirely, enter into solution, as well as traces of brucine, narcotine, physostigmine, veratrine, delphinine. The evaporation of the chloroform is conducted at the ordinary temperature in four or five watch-glasses.

THE CHLOROFORM RESIDUE FROM THE ACID SOLUTION.

1. THE RESIDUE IS MORE OR LESS MARKEDLY CRYSTALLINE.

A. *It gives in the sulphuric acid solution evidence of an alkaloid by its action towards iodine and iodide of potash.*

α. Sulphuric acid dissolves it without the production of colour, and chlorine and ammonia give no murexide reaction. *Cinchonine.*

β. Sulphuric acid dissolves it without colour, chlorine and am-

A. *In acetic acid solution it renders the action of the frog's heart slower, or produces local anaesthesia.*

αα. It does not produce local anaesthesia.

α. Sulphuric acid dissolves it red-brown, bromine produces a beautiful purple colour, water changes it into green, hydrochloric acid dissolves it into greenish-brown.

Digitalin.

β. Sulphuric acid dissolves it yellow, then brown-red; on addi-

ia give, as with theine, a mur-
e reaction.

Theobromine.

tion of water this solution becomes
violet. Hydrochloric acid, on
warming, dissolves it red.

Convallamarin.

bb. It produces local anæsthe-
sia.

α. Sulphuric acid dissolves it
brown. The solution becomes, by
extracting with water, violet, and
can even be diluted with two vol-
umes of water without losing its
colour.

Saponin.

β. Sulphuric acid dissolves it
yellow. On diluting with water
the same reaction occurs as in the
previous case, but more feebly.

Senegin.

γ. Sulphuric acid dissolves
brown, and the solution becomes
red by the addition of a little water.

The action is very weak.

Papaverine.

Smilacin.

cc. Sulphuric acid dissolves it
with the production of a dirty red,
hydrochloric acid, in the cold,
with that of a reddish-brown col-
our, and the last solution becomes
brown on boiling.

*Constituents of the hellebore,
particularly Jervin.*

Sulphuric acid dissolves it in
cold with the production of a
colour.

*Unknown impurities, many
commercial samples of Pa-
paverine.*

Sulphuric acid dissolves it at
grey-brown ; the solution be-
sins about twenty-four hours
-red. Iodine water colours it

Narceine.

IT GIVES NO ALKALOID RE-
CN.

b. It is inactive, and becomes
blue by sulphuric acid; by Fröhde's

reagent * dark cherry-red. Hydrochloric acid dissolves it red. The solution becomes, by boiling, colourless. *Syringin.*

α . Sulphuric acid dissolves it with a beautiful yellow colour; mixed with nitre, then moistened with sulphuric acid, and lastly treated with concentrated soda-lye, it is coloured a brick-red.

Picrotoxin.

β . Sulphuric acid dissolves it with the production of a splendid red colour. The substance renders the heart-action of a frog slower.

Helleborin.

VI. THE WATERY FLUID IS NOW AGAIN SHAKEN UP
WITH PETROLEUM ETHER,

in order to take up the rest of the chloroform, and the watery fluid is saturated with ammonia. The watery solution of *aconitine* and *emetin* is liable to undergo, through free ammonia, a partial decomposition; but, on the other hand, it is quite possible to obtain, with very small mixtures of these substances, satisfactory reactions, even out of ammoniacal solutions.

VII. THE AMMONIACAL WATERY FLUID WITH PETROLEUM ETHER.

In the earlier stages Dragendorff advises the shaking up with petroleum ether at about 40° , and the removal of the ether as quickly as possible whilst warm. This is with the intention of separating by this fluid strychnine, brucine, emetin, quinine, veratrine, &c. Finding, however, that a full extraction by petroleum ether is either difficult or not practicable, he prefers, as we have seen, to conclude the operation by other agents, coming back again upon the ether for certain special cases. Such are the volatile alkaloids; and here he recommends treatment of the fluid by *cold* petroleum ether, taking care *not* to hasten the removal of the latter. Strychnine and other fixed alkaloids are then only taken up in small quantities, and the greater portion remains for the later treatment of the watery fluid by benzene.

* Described at page 211.

A portion of the petroleum ether, supposed to contain in solution volatile alkaloids, is evaporated in two watch-glasses; to the one, strong hydrochloric acid is added, the other being evaporated without this agent. On the evaporation of the petroleum ether, it is seen whether the first portion is crystalline or amorphous, or whether the second leaves behind a strongly-smelling fluid mass, which denotes a volatile alkaloid. If the residue in both glasses is without odour and fixed, the absence of volatile acid and the presence of fixed alkaloids, strychnine, emetin, veratrine, &c., are indicated.

THE PETROLEUM ETHER RESIDUE FROM AMMONIACAL SOLUTION.

1. IT IS FIXED AND CRYSTALLINE.

A. The crystals are volatilised with difficulty.

aa. Sulphuric acid dissolves it without colour.

a. Potassic chromate colours this solution a transitory blue, then red.

Strychnine.

β. Potassic chromate does not colour it blue; with chlorine water and ammonia it gives a green colour.

Quinine.

2. IT IS FIXED AND AMORPHOUS.

a. The purest sulphuric acid dissolves it almost without colour; sulphuric containing nitric acid, red quickly becoming orange.

Brucine.

β. Sulphuric acid dissolves it yellow, becoming deep red.

Veratrine.

γ. Sulphuric acid dissolves it brown-green; Fröhde's re-

3. IT IS FIXED AND ODOROUS.

A. On adding to the watch-glass a little hydrochloric acid, crystals are left behind.

aa. Its solution is not precipitated by platin chloride.

a. The crystals of the hydrochloric compound act on polarised light; and are mostly needle-shaped and columnar.

Coniine and Methyl-coniine.

β. The crystals are cubical or tetrahedral.

Alkaloid from Capsicum.

agent red, changing into green.

Emetin.

bb. The solution of the hydrochlorate of the alkaloid is precipitated by platin chloride.

Sarracinin.

b. The residue of the hydrochlorate of the alkaloid is amorphous, or, by further additions of HCl, becomes crystalline.

b. Sulphuric acid dissolves it yellow, and the solution becomes gradually a beautiful deep red.

Sabadilline.

c. The crystals are easily volatilised.

Coniine.

aa. Its diluted aqueous solution is precipitated by platin chloride.

a. The hydrochlorate salt, being quickly treated with Fröhde's reagent, gives after about two minutes a deep violet solution which gradually fades.

Lobeliin.

β. The hydrochlorate smells like nicotine, and becomes by Fröhde's reagent yellow, and after twenty-four hours pale red.

Nicotine.

The hydrochlorate is without odour, the free base smells faintly like aniline.

Sparteine.

bb. The substance is not precipitated from a diluted solution by platin chloride.

α. Its petroleum ether solution produces no turbidity with a solution of picric acid in petroleum ether; but it leaves behind, when mixed with the above, crystals mostly of three-sided plates.

Trimethylamine.

β. The petroleum ether solution gives, on evaporation, when treated similarly, moss-like crystals. The substance is made blue by chloride of lime, as well as by diluted sulphuric acid and bichromate of potash.

Aniline.

γ. The alkaloid does not smell like methylamine, and is not coloured by chloride of lime, sulphuric acid, or chromate of potash.

Volatile alkaloid of the Pimento.

II. THE AMMONIACAL SOLUTION IS SHAKEN UP WITH BENZENE.

In most cases petroleum ether, benzene, and chloroform, are more easily separated from acid watery fluids than from ammoniacal, benzene

and chloroform causing here a difficulty which has perhaps deterred many from using this method. Dragendorff, however, maintains that he has never examined a fluid in which he could not obtain a complete separation of the benzene and water. If the upper benzene layer is fully gelatinous and emulsive, the under layer of water is to be removed with a pipette as far as possible, and the benzene with a few drops of absolute alcohol and filtration. As a rule, the water goes through first alone, and by the time the greater part has run through, the jelly in the filter, by dint of stirring, has become separated from the benzene, and, finally, the jelly shrinks up to a minimum, and the clear benzene filters off. Dragendorff filters mostly into a burette, from which ultimately the benzene and the water are separated.

The principal alkaloids which are dissolved in benzene are—strychnine, methyl and ethyl strychnine, brucine, emetin, quinine, cinchonine, atropine, hyoscyamine, physostigmine, aconitine, nepalin, the alkaloid of the *Aconitum lycoctonum*, aconellin, napellin, delphinine, veratrine, sabatrin, sabadilline, codeine, thebaine, and narcotine.

THE BENZENE RESIDUE DERIVED FROM THE AMMONIACAL SOLUTION.

1. IT IS FOR THE MOST PART CRYSTALLINE.

a. Sulphuric acid dissolves it without colour, the solution being coloured neither on standing nor on the addition of nitric acid.

aa. It dilates the pupil of a cat.

α. Platin chloride does not precipitate the aqueous solution. The sulphuric acid solution gives, on warming, a peculiar smell.

Atropine.

β. Platin chloride applied to the solution precipitates.

Hyoscyamine.

bb. It does not dilate the pupil.

α. The sulphuric acid solution becomes blue by chromate of potash.

αα. The substance applied to a frog produces tetanus.

Strychnine.

2. IT IS FOR THE MOST PART AMORPHOUS.

a. Pure sulphuric acid dissolves it either whitish-red or yellowish.

α. The solution becomes by nitric acid immediately red, then quickly orange. *Brucine.*

β. The solution becomes by little and little brownish-red. The substance is coloured red by chloride of lime solution, and it contracts the pupil. *Physostigmine.*

$\beta\beta$. It lowers the number of respirations in a frog.

Ethyl and Methyl Strychnine.

β . Sulphuric acid and bichromate of potash do not colour it blue.

$\alpha\alpha$. The sulphuric acid watery solution is fluorescent, and becomes green on the addition of chlorine water and ammonia.

Quinine and Cinchonine.

(The last is more difficult to dissolve in petroleum ether than quinine.)

$\beta\beta$. The solution is not fluorescent.

Cinchonine.

b . Sulphuric acid dissolves it at first colourless ; the solution takes on standing a rose or violet-blue ; on addition of nitric acid, a blood-red or brown coloration.

α . A solution in diluted sulphuric acid becomes, on heating, gradually deep blood-red, and, when cooled, violet, with nitric acid. The aqueous solution is precipitated by ammonia.

Narcotine.

b . Pure sulphuric acid dissolves it yellow, and the solution becomes later beautiful red with delphinine, more quickly a darker cherry-red).

α . The hydrochloric acid solution becomes red on heating.

$\alpha\alpha$. The substance acts on a frog, causing, in large doses, tetanus.

Veratrine.

It is almost without action on frogs.

Sabatin.

β . The hydrochloric acid solution does not, on heating, become red.

Delphinine.

β . The solution in diluted sulphuric acid becomes, on heating, a beautiful blue. Excess of ammonia does not precipitate in a diluted watery solution.

Codeine.

c . Sulphuric acid dissolves it with the production of a yellow colour.

α . The solution remains yellow on standing.

Acolyctin.

c . Pure sulphuric acid dissolves it yellow, and the solution becomes later red-brown, and gradually violet-red.

α . The substance even in small doses paralyses frogs, and dilates

the pupil of a cat's eye. Ether dissolves it with difficulty. *Nepalin.*

β. It becomes beautifully red.

Sabadilline.

β. It is easily soluble in ether, its effects are not so marked, and it does not dilate the pupil.

Aconitine.

Its effects are still feeble; it does not dilate the pupil, and is with difficulty dissolved by ether.

Napellin.

d. Sulphuric acid dissolves it with an immediate deep red-brown colour.

Thebaine.

d. Sulphuric acid dissolves it with a dark green colour, and the solution becomes, even after a few seconds, a beautiful blood-red.

Alkaloidal substances out of the Aconitum lycoctonum.

e. Sulphuric acid dissolves it immediately blue.

Substances accompanying the Papaverins.

e. Sulphuric acid dissolves it brown-green, and Fröhdes reagent red, becoming beautifully green.

Emetin.

IX. SHAKING OF THE AMMONIACAL WATERY SOLUTION WITH CHLOROFORM.

This extracts the remainder of the cinchonine and papaverine, narceine, and a small portion of morphine, as well as an alkaloid from the celandine.

THE RESIDUE FROM THE CHLOROFORM.

aa. The solution, on warming, is only slightly coloured.

α. But after it is again cooled, it strikes with nitric acid a violet-blue; chloride of iron mixed with the substance gives a blue colour; Fröhde's reagent also dissolves it violet.

Morphine.

β. It is not coloured by nitric acid; it is also indifferent to chloride of iron.

Cinchonine.

bb. The solution becomes by warming violet-blue.

Papaverine.

β. Sulphuric acid dissolves it greenish-brown, and the solution becomes, on standing, blood-red.

Narceine

β. Sulphuric acid dissolves it a violet-blue.

Alkaloidal constituent of the Celandine.

X. SHAKING UP OF THE WATERY FLUID WITH AMYL ALCOHOL.

From this process, besides morphine and solanine, as well as salicin, the remnants of the convallamarin, saponine, senegin, and narceine, are also to be expected.

THE AMYL ALCOHOL RESIDUE.

a. Sulphuric acid dissolves it without colour in the cold.

Morphine (see above).

b. Sulphuric acid dissolves it with the production of a clear yellow-red, and the solution becomes brownish. Iodine water colours it a deep brown. The alcoholic solution gelatinises. *Solanine*.

c. Sulphuric acid dissolves it green-brown, becoming red.

Narceine (see above.)

d. Sulphuric acid dissolves it yellow, then brown-red, becoming violet on dilution with water. Hydrochloric acid dissolves it, and it becomes red on warming. It stops the heart-action in the systole.

Convallamarin.

β. Hydrochloric acid dissolves it for the most part without colour.

Saponin

γ. As the foregoing, but acting more feebly.

Senegin.

e. Sulphuric acid dissolves it immediately a pure red. On warming with sulphuric acid and bichromate of potash, a smell of salicylic acid is developed. *Salicin*.

XI. DRYING THE WATERY FLUID WITH THE ADDITION OF POWDERED GLASS, AND EXTRACTION OF THE FINELY-DIVIDED RESIDUE BY CHLOROFORM.

The residue of the first chloroform extract lessens the number of respirations of a frog; the residue of the second and third chloroform extract becomes, by sulphuric acid and bichromate of potash, blue, passing into a permanent red.

Another portion of this residue becomes red on warming with diluted sulphuric acid. *Curarine*.

SHORTER PROCESS FOR SEPARATING SOME OF THE ALKALOIDS.

A shorter process, recommended conditionally by Dragendorff, for brucine, strychnine, quinine, cinchonine, and emetin, is as follows:—

The substance, if necessary, is finely divided, and treated with sulphuric acid (dilute) until it has a marked acid reaction. To every 100 cc.

of the pulp (which has been diluted with distilled water to admit of being filtered later), at least 5 to 10 cc. of diluted sulphuric acid (1 are added. It is digested at 50° for a few hours, filtered, and the residue treated again with 100 cc. of water at 50°. This extract is, after a few hours, again filtered; both the filtrates are mixed and evaporated in a water-bath to almost the consistency of a thin syrup. The fluid, however, must not be concentrated too much, or fully evaporated to dryness. The residue is now placed in a flask, and treated with three to four times its volume of alcohol of 90 to 95 per cent.; the mixture is macerated for twenty-four hours, and then filtered. The filtrate is distilled alcohol-free, or nearly so, but a small amount of alcohol remaining is not objectionable. The watery fluid is diluted to about 50 cc., and treated with pure benzene; the mixture is shaken, and after a little time the benzene removed—an operation which is repeated. After the removal of the benzene, the watery fluid is made alkaline with ammonia, and warmed to 40° to 50°, and the free alkaloid extracted by twice shaking up with two different applications of benzene. On evaporation of the latter, if the alkaloid is not left pure, it can be dissolved in acid, precipitated by ammonia, and again extracted by benzene. See also the process recommended at page 210.

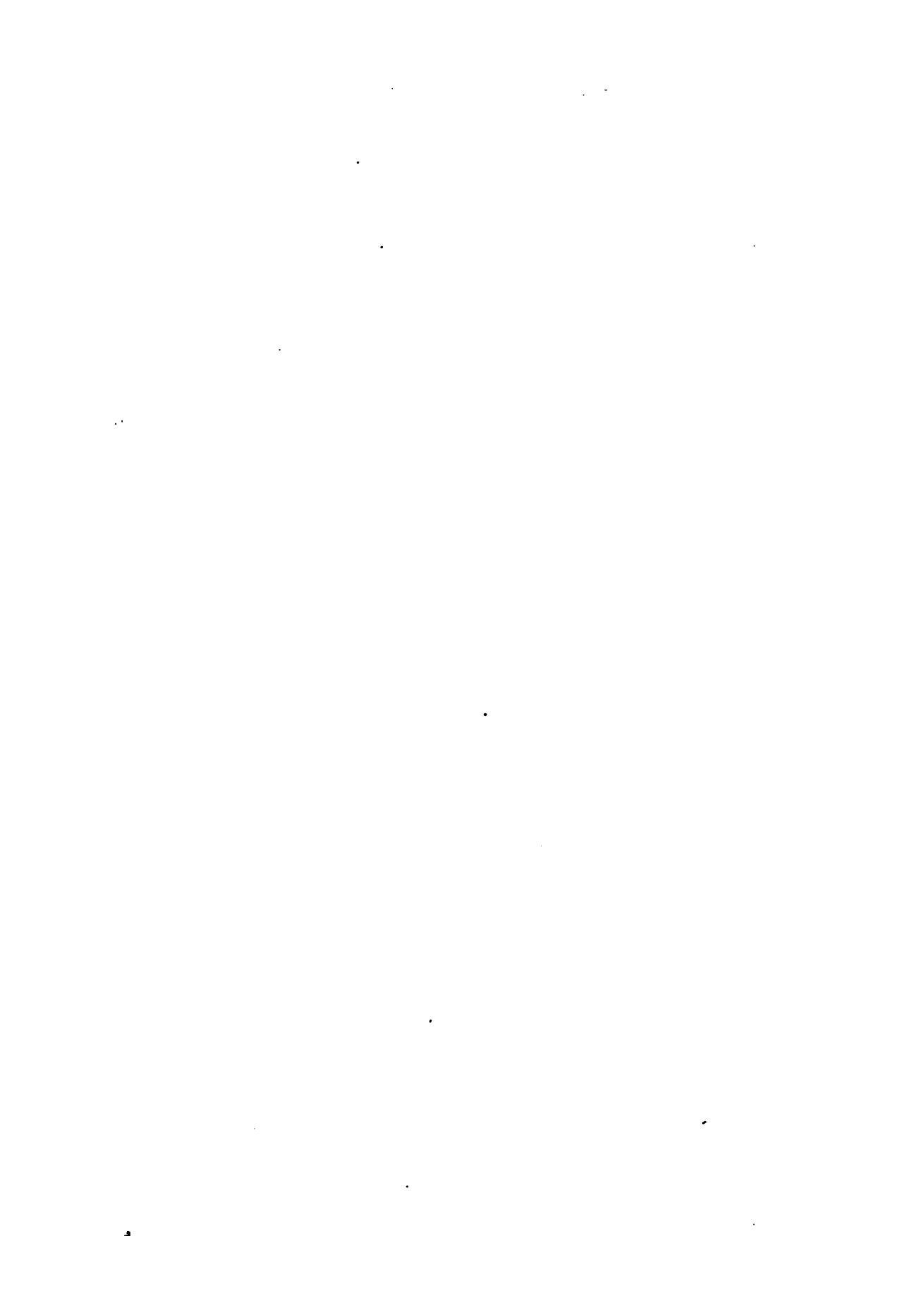
Scheibler's Process.—A method very different from those just described is one practised by Scheibler. This is to precipitate the phosphotungstate of the alkaloid, and then to liberate the latter by digesting the precipitate with either hydrate of barium or hydrate of calcium, dissolving it out by chloroform, or, if volatile, by simple distillation. The convenience of Scheibler's process is great, and it admits of very general application. In complex mixtures, it will usually be found best to precede the addition of phosphotungstic acid* by that of acetate of lead in order to remove colouring matter, &c.; the excess of lead must in turn be thrown out by SH_2 , and the excess of SH_2 be got rid of by evaporation. Phosphotungstic acid is a very delicate test for the alkaloids, giving a distinct precipitate with the most minute quantities ($\frac{1}{200000}$ of strychnine and $\frac{1}{100000}$ of quinine). A very similar method is practised by Sonnenschmid and others with the aid of phosphomolybdic acid. The details of Scheibler's process are as follows:—

The organic mixture is repeatedly extracted by water strongly acidified with sulphuric acid; the extract is evaporated at 30° to the consistency of a thin syrup, then diluted with water, and, after several hours standing, filtered in a cool place. To the filtered fluid phosphotungstic

*The method of preparing this reagent is as follows:—Ordinary commercial sodium tungstate is treated with half its weight of phosphoric acid, specific gravity 1.18, and then allowed to stand for some days. Phosphotungstic acid separates in crystals.

S.

	Ferric Chloride.	Other Reactions.
	In watery solution is precipitated yellow.	The precipitate with phosphomolybdic acid soon becomes blue.
	Is not precipitated.	Dilates the pupil.
	Berberine dissolved in a little HCl and a few drops of chlorine water becomes red.
	Boiling perchloric acid colours in Madeira red. In diluted sulphuric acid (1:8) a little potassio chromate colours it a beautiful red.
	Chelidoneine is not poisonous—the hydrochlorate forms fine crystals, soluble in 324 parts of water, and precipitated by concentrated HCl.
	Is not precipitated.	Does not become green with the chlorine ammonia test.
	Is not precipitated.	Does not become green with the chlorine ammonia test.
	The precipitate with chloride of gold is quickly decomposed with production of a red colour. The solution in sulphuric acid, to which nitric acid has been added after disappearance of a blue colour, is reddened by potash.
	Gives a crystalline residue with HCl.
1 red.		
	The sulphuric acid solution becomes violet with bromine.
	Concentrated hydrochloric acid colours the solution in Fröhde's reagent deep blue.
	Is not precipitated.	Dilates the pupil.
	Colourless.	On warming with sulphuric acid and a little ferric chloride, it becomes blue.
	Blue.	Reduces iodate, silver nitrate—reddens ferrocyanide, &c.
	A beautiful red colour on evaporating the solution in dilute sulphuric acid.
	Evaporated with dilute HCl gives an amorphous residue.
	On warming with sulphuric acid becomes blue.
	Is coloured red by calcio chloride solution; mercuric iodide precipitate soluble in alcohol.
	In hydrochloric acid solution is precipitated.	
	Is not precipitated.	Solution in chlorine water becomes green on the addition of ammonia.
1 pale.	Brown precipitate.	The blue colour is more vivid with sulphuric acid and cerium oxide.
	Chloride of gold and taxin is easily soluble.
	Is not precipitated.	Dissolved in chlorine water on evaporation gives a red brown residue, coloured red by ammonia.
	Gives a precipitate in HCl solution.	



acid is added in excess, the precipitate filtered, washed with water to which some phosphotungstic acid and H_2N_2 have been added, and, whilst still moist, rinsed into a flask. Caustic baryta or carbonate of potash is added to alkaline reaction, and after the flask has been connected with bulbs containing HCl , it is heated at first slowly, then more strongly. Ammonia and any volatile alkaloids are driven over into the acid, and are there fixed, and can be examined later by suitable methods. The residue in the flask is carefully evaporated to dryness (the excess of baryta having been precipitated by CO_2), and then extracted by strong alcohol. On evaporation of the alcohol, the alkaloid is generally sufficiently pure to be examined, or, if not so, it may be obtained pure by re-solution, &c.

I have had considerable experience of Scheibler's process, and have used it in precipitating various animal fluids, but have generally found the precipitate bulky and difficult to manage.

Identification of the Alkaloids.—Having obtained, in one way or other, a crystalline or amorphous substance, supposed to be an alkaloid, or, at all events, an active vegetable principle, the next step is to identify it. If the tests given in Dragendorff's process have been applied, the observer will have already gone a good way towards the identification of the substance ; but it is, of course, dangerous to trust to one reaction.

In medico-legal researches there is seldom any considerable quantity of the material to work upon. Hence the greatest care must be taken from the commencement not to waste the substance in useless tests, but to study well at the outset what—by the method of extraction used, the microscopic appearance, the reaction to litmus paper, and the solubility in different menstrua—it is likely to be. However minute the quantity may be, it is essential to divide it into different parts, in order to apply a variety of tests ; but as any attempt to do this on the solid substance will probably entail loss, the best way is to dissolve it in a watch-glass in half a cc. of alcohol, ether, or other suitable solvent. Droplets of this solution are then placed on watch-glasses or slips of microscopic glass, and to these drops, by the aid of a glass rod, different reagents can be applied, and the changes watched under the microscope as the drops slowly evaporate.

Colour Reactions.—Alkaloids, when fairly pure, have certain colour reactions more or less characteristic, when the solid substance is mixed with the mineral acids, Fröhde's reagent, sulphuric acid, and potassic bichromate. The following table gives a summary of the more important results of these tests. Colour reactions generally are untrustworthy, but must be looked upon as useful guides only, to be confirmed by the other characteristics of the substance :—

Sublimation of the Alkaloids.—A very beautiful and elegant aid to the identification of alkaloids, and vegetable principles generally, is their behaviour towards heat.

Alkaloids, glucosides, the organic acids, &c., when carefully heated, either—(1) sublime wholly without decomposition (like theine, cytisin, and others); or (2) partially sublime with decomposition; or (3) are changed into new bodies (as, for example, gallic acid); or (4) melt and then char; or (5) simply char and burn away.

Many of these phenomena are striking and characteristic, taking place at definite temperatures, subliming in characteristic forms or leaving characteristic residues.

One of the first to employ sublimation systematically, as a means of recognition of the alkaloids, &c., was Helwig.* His method was to place a small quantity (from $\frac{1}{2}$ to $\frac{1}{4000}$ of a milligram) in a depression on platinum foil, cover it with a slip of glass, and then carefully heat by a small flame. After Helwig, Dr. Guy † greatly improved the process by using porcelain discs, and more especially by the adoption of a convenient apparatus, which may be termed "the subliming cell." It is essentially composed of a ring of glass from $\frac{1}{8}$ to $\frac{2}{3}$ of an inch in thickness, such as may be obtained by sections of tubing, the cut surfaces being ground perfectly smooth. This circle is converted into a closed cell by resting it on one of the ordinary thin discs of glass used as a covering for microscopic purposes, and supporting a similar disc. The cell was placed on a brass plate, provided with a nipple, which carried a thermometer, and was heated by a small flame applied mid-way between the thermometer and the cell; the heat was raised very gradually, and the temperature at which any change took place was noted. In this way Dr. Guy made determinations of the subliming points of a large number of substances, and the microscopic appearances of the sublimates were described with the greatest fidelity and accuracy. On repeating with care Dr. Guy's determinations, however, I could in no single instance agree with his subliming points, nor with the apparatus he figures and describes could two consecutive observations exactly coincide. Further, on examining the various subliming temperatures of substances, as stated by different authors, the widest discrepancies were found—differences of two or even three degrees might be referred to errors of observation, a want of exact coincidence in the thermometers employed, and the like; but to what, for example, can we ascribe the irreconcilable statements which have been made with regard to theine? According to Stranch, this substance sublimes at 177° ; according to Mulder, at 184.7° . But that both of these observations deviate more than 70° from the truth may be proved

* *Das Mikroskop in der Toxicologie.*

† *Pharm. Journ. Trans.* [2], viij. 719; ix. 10, 58. "Forensic Medicine," London, 1875.

by any one who cares to place a few milligrams of theine, enclosed between two watch-glasses, over the water-bath ; in a few minutes a distinct sublimate will condense on the upper glass, and, in point of fact, theine will be found to sublime several degrees below 100°.

Since this great divergency of opinion is not found either in the specific gravity, or the boiling points, or any of the like determinations of the physical properties of a substance, it is self-evident that the processes hitherto used for the determination of subliming points are faulty. The sources of error are chiefly—

(1.) Defects in the apparatus employed—the temperature read being rather that of the metallic surface in the immediate vicinity of the thermometer than of the substance itself.

(2.) The want of agreement among observers as to what should be called a sublimate—one considering a sublimate only that which is evident to the naked eye; another taking cognisance of the earliest microscopic film.

(3.) No two persons employing the same process.

With regard to the apparatus employed, I adopt Dr. Guy's subliming cell ; but the cell, instead of resting on a metallic solid, floats on a metallic fluid. For any temperature a little above 100° this fluid is mercury, but for higher temperatures fusible metal is preferable.



Fig. 13.

The exact procedure is as follows :—A porcelain crucible (see Fig. 13, *a*), about 3 inches in diameter, is nearly filled with mercury or fusible metal, as the case may be ; a minute speck (or two or three crystals of the substance to be examined) is placed on a thin disc of microscopic covering glass, floated on the liquid, and the cell is completed by the glass ring and upper disc. The porcelain crucible is supported on a brass plate (*b*), fixed to a retort stand in the usual way, and protected from the unequal cooling effects of currents of air by being covered with a flask (*c*), from which the bottom has been removed. The neck of the flask conveniently supports a thermometer, which passes through a cork, and the bulb of the thermometer is immersed in the bath of liquid metal. In the first examination of a substance the temperature is

raised somewhat rapidly, taking off the upper disc with a forceps at every 0° and exchanging it for a fresh disc, until the substance is destroyed. The second examination is conducted much more slowly, and the disc exchanged at every 4° or 5°, whilst the final determination is effected by

raising the temperature with great caution, and exchanging the discs at about the points of change (already partially determined) at every half degree. All the discs are examined microscopically. The most convenient definition of a sublimate is this—the most minute films, dots, or crystals, which can be observed by $\frac{1}{4}$ -inch power, and which are obtained by keeping the subliming cell at a definite temperature for sixty seconds. The commencement of many sublates assumes the shape of dots of extraordinary minuteness, quite invisible to the unaided eye; and, on the other hand, since the practical value of sublimation is mainly as an aid to other methods for the recognition of substances, if we go beyond short intervals of time, the operation, otherwise simple and speedy, becomes cumbersome, and loses its general applicability.

There is also considerable discrepancy of statement with regard to the melting point of alkaloidal bodies; in many instances a viscous state intervenes before the final complete resolution into fluid, and one observer will consider the viscous state, the other complete fluidity, as the melting point.

In the melting points given below, the same apparatus was used, but the substance was simply placed on a thin disc of glass floating on the metallic bath before described (the cell not being completed), and examined from time to time microscopically, for by this means alone can the first drops formed by the most minute and closely adherent crystals to the glass be discovered.

Morphine, at 150° , clouds the upper disc with nebulae; the nebulae are resolved by high magnifying powers into minute dots; these dots gradually become coarser, and are generally converted into crystals at 188° ; the alkaloid browns at or about 200° .

Thebaine sublimes in theine-like crystals at 135° ; at higher temperatures (160° to 200°), needles, cubes, and prisms are observed. The residue on the lower disc, if examined before carbonisation, is fawn-coloured with non-characteristic spots.

Narcotine gives no sublimate; it melts at 155° into a yellow liquid, which, on raising the temperature, ever becomes browner to final blackness. On examining the residue before carbonisation, it is a rich brown amorphous substance; but if narcotine be heated two or three degrees above its melting point, and then cooled slowly, the residue is crystalline—long, fine needles radiating from centres being common.

Narceine gives no sublimate; it melts at 134° into a colourless liquid, which undergoes at higher temperatures the usual transition of brown colours. The substance, heated a few degrees above its melting point, and then allowed to cool slowly, shows a straw-coloured residue, divided into lobes or drops containing feathery crystals.

Papaverine gives no sublimate; it melts at 130° . The residue,

heated a little above its melting point, and then slowly cooled, is amorphous, of a light-brown colour, and in no way characteristic.

Hyoscyamine gives no crystalline sublimate ; it melts at 89° , and appears to volatilise in great part without decomposition. It melts into an almost colourless fluid, which, when solid, may exhibit a network not unlike vegetable parenchyma ; on moistening the network with water, interlacing crystals immediately appear. If, however, hyoscyamine be kept at 94° to 95° for a few minutes, and then slowly cooled, the edges of the spots are arborescent, and the spots themselves crystalline.

Atropine (daturine) melts at 97° ; at 123° a faint mist appears on the upper disc. Crystals cannot be obtained ; the residue is not characteristic.

Solanine.—The upper disc is dimmed with nebulae at 190° , which are coarser and more distinct at higher temperatures ; at 200° it begins to brown, and then melts ; the residue consists of amber-brown, non-characteristic drops.

Strychnine gives a minute sublimate of fine needles, often disposed in lines, at 169° ; about 221° it melts, the residue (at that temperature) is resinous.

Brucine melts at 151° into a pale yellow liquid, at higher temperatures becoming deep-brown. If the lower disc, after melting, be examined, no crystals are observed, the residue being quite transparent, with branching lines like the twigs of a leafless tree ; light mists, produced rather by decomposition than by true sublimation, condense on the upper disc at 185° , and above.

Saponin neither melts nor sublimes ; it begins to brown about 145° , is almost black at 185° , and quite so at 190° .

Delphinine begins to brown about 102° ; it becomes amber at 119° , and melts, and bubbles appear. There is no crystalline sublimate ; residue not characteristic.

Pilocarpine gives a distinct crystalline sublimate at 153° ; but thin mists, consisting of fine dots, may be observed as low as 140° . *Pilocarpine* melts at 159° ; the sublimates at 160° to 170° are in light yellow drops. If these drops are treated with water, and the water evaporated, feathery crystals are obtained ; the residue is resinous.

Theine wholly sublimes ; the first sublimate is minute dots, at 79° ; at half a degree above that very small crystals may be obtained ; and at such a temperature as 120° , the crystals are often long and silky.

Theobromine likewise wholly sublimes ; nebulae at 134° , crystals at 170° , and above.

Salicin melts at 170° ; it gives no crystalline sublimate. The melted mass remains up to 180° ; almost perfectly colourless ; above that temperature browning is evident. The residue is not characteristic.

Picrotoxin gives no crystalline sublimate. The lowest temperature at which it sublimes is 128° ; the usual nebulæ then make their appearance; between 165° and 170° degrees there is slight browning; at 170° it melts. The residue, slowly cooled, is not characteristic.

Cantharidin sublimes very scantily between 82° and 83° ; at 85° the sublimate is copious.

The active principles of plants may, in regard to their behaviour to heat, be classed for practical purposes into—

1. Those which give a decided crystalline sublimate:

- (a.) Below 100° , e.g., theine, thebaine, cantharidin.
- (b.) Between 100° and 150° , e.g., quinetum.
- (c.) Between 150° and 200° , e.g., strychnine, morphine, pilocarpine.

2. Those which melt, but give no crystalline sublimate :

- (a.) Below 100° , e.g., hyoscyamine, atropine.
- (b.) Between 100° and 150° , e.g., papaverine.
- (c.) Between 150° and 200° , e.g., salicin.
- (d.) Above 200° , e.g., solanine.

3. Those which neither melt nor give a crystalline sublimate, e.g., saponin.

Identification by Organic Analysis.—In a few cases (and in a few only) the analyst may have sufficient material at hand to make an organic analysis, either as a means of identification or to confirm other tests. By the vacuum process described in vol. i., "Foods," in which carbon and nitrogen are determined by measuring the gases evolved by burning the organic substance in as complete a vacuum as can be obtained, very minute quantities of a substance can be dealt with, and the carbon and nitrogen determined with great accuracy. It is found in practice that the carbon determinations appear more reliable than those of the nitrogen, and there are obvious reasons why this should be so.

Theoretically, with the approved gas-measuring appliances, it is possible to measure a cc. of gas; but few chemists would care to create a formula on less than 10 cc. of CO_2 . Now, since 10 cc. of CO_2 is equal to 6.33 mgrms. of carbon, and alkaloids average at least half their weight of carbon, it follows that 12 mgrms. of alkaloid represent about the smallest quantity with which a reliable single combustion can be made.

The following table gives a considerable number of the alkaloids and alkaloidal bodies, arranged according to their content in carbon:—

TABLE VII.—CONTENT OF CARBON AND NITROGEN IN
VARIOUS ALKALOIDAL BODIES.

	Carbon.	Nitrogen.
Asparagin, .	86.86	21.21
Methylamine, .	88.71	45.17
Betaine, .	44.44	10.87
Theobromine, .	46.67	81.11
Theine, .	49.48	28.86
Indican, .	49.60	2.22
Muscarine, .	50.42	11.77
Lauro-cerasin, .	52.47	1.53
Amanitine, .	57.69	18.46
Narceine, .	59.63	8.02
Colchicine, .	60.53	4.15
Oxyacanthine, .	60.57	4.42
Solanine, .	60.66	1.68
Trimethylamine, .	61.02	28.73
Jervine, .	61.08	5.14
Sabadilline, .	61.29	8.46
Aconitine, .	61.39	2.17
Nepaline, .	63.09	2.12
Colchicein, .	63.44	4.88
Veratroidine, .	63.8	8.1
Narcotine, .	63.92	8.39
Veratrine, .	64.42	2.91
Belphinine, .	64.55	8.42
Physostogmine, .	65.49	15.27
Rhœadine, .	65.79	8.65
Cocaine, .	66.44	4.84
Gelsemine, .	67.00	7.10
Conhydrine, .	67.12	9.79
Staphisagrine, .	67.5	8.6
Chelidone, .	68.06	12.34
Atropine, Hyoscyamine, .	70.58	4.84
Sanguinarine, .	70.59	4.83
Papaverine, .	70.79	4.18
Delphinoidine, .	70.9	8.9
Morphine and Piperine, .	71.58	4.91
Berberine, .	71.64	4.18
Codeine, .	72.24	4.68
Thebaine, .	73.31	4.50
Cytisine, .	73.85	12.92
Nicotine, .	74.08	17.28
Quinine, .	75.02	8.64
Coniine, .	76.81	11.20
Strychnine, .	77.24	8.92
Curarine, .	81.51	5.28

Quantitative Estimation of the Alkaloids.—For medico-legal purposes

the alkaloid obtained is usually weighed directly, but for technical purposes other processes are used. One of the most convenient of these is titration with normal or decinormal sulphuric acid, a method applicable to a few alkaloids of marked basic powers—*e. g.*, quinine is readily and with accuracy estimated in this way, the alkaloid being dissolved in a known volume of the acid, and then titrated back with soda. If a large number of observations are to be made, an acid may be prepared so that each cc. equals 1 mgrm. of quinine. A reagent of general application is found in the so-called *Mayer's reagent*, which consists of 13,546 grms. of mercuric chloride, and 49.8 grms. of iodide of potash in the litre of water. Each cc. of such solution precipitates—

Of Strychnine,	·0167 grm.
" Brucine,	·0233 "
" Quinine,	·0108 "
" Cinchonine,	·0102 "
" Quinidine,	·0120 "
" Atropine,	·0145 "
" Aconitine,	·0268 "
" Veratrine,	·0269 "
" Morphine,	·0200 "
" Narcotine,	·0213 "
" Nicotine,	·00405 "
" Coniine,	·00416 "

The final reaction is found by filtering, from time to time, a drop on to a glass plate, resting on a blackened surface, and adding the test until no precipitate appears. The results are only accurate when the strength of the solution of the alkaloid is about 1 : 200 ; so that it is absolutely necessary first to ascertain approximatively the amount present, and then to dilute or concentrate, as the case may be, until the proportion mentioned is obtained.

A convenient method of obtaining the sulphate of an alkaloid for quantitative purposes, and especially from organic fluids, is that recommended by Wagner. The fluid is acidulated with sulphuric acid, and the alkaloid precipitated by a solution of iodine in iodide of potash. The precipitate is collected and dissolved in an aqueous solution of hyposulphite of soda. The filtered solution is again precipitated with the iodine reagent, and the precipitate dissolved in sulphurous acid, which, on evaporation, leaves behind the pure sulphate of the base.

It is also very useful for quantitative purposes to combine an alkaloid with gold or platinum, by treating the solution with the chlorides of either of those metals—the rule as to selection being to give that metal the preference which yields the most insoluble and the most crystallisable compound.

The following table gives the percentage of gold or platinum left on ignition of the double salt :

TABLE VIII.

	Gold.	Platinum.
Atropine,	31.57	...
Aconitine,	22.06	...
Amanitine,	44.23	...
Berberine,	29.16	18.11
Brucine,	16.52
Cinchonine,	27.36
Cinchonidine,	27.87
Codeine,	19.11
Coniine,	29.38
Curarine,	32.65
Delphinine,	26.7	...
Delphinoidine,	29.0	15.8
Emetin,	29.7
Hyoscyamine,	34.6	...
Morphine,	19.52
Muscarine,	43.01	...
Narcotine,	15.7	15.9
Narceine,	14.52
Nicotine,	34.25
Papaverine,	17.82
Pilocarpine,	35.5	23.6 to 25.2
Piperine,	12.7
Quinine,	40.0	26.26
Strychnine,	29.15	18.16
Thebaine,	18.71
Theine,	37.02	24.58
Theobromine,	25.58
Veratrine,	21.01	...

*Baroptic Estimation.**—If W be the weight of a body, V its volume, S its specific gravity, and U the weight of a unit of the standard, then $W = VSU$. This well-known principle is constantly applied to determine the weight of large masses of substances, which, from their bulk or position, cannot be directly placed on a balance—for example, the Egyptian pyramids have been measured, and the weights calculated from the cubic volume and the known specific gravity of the stone entering into their composition. If the formula has thus been made use of in the *vast*, it is also applicable to the *minute*—to small particles of substances, so fine that they are inappreciable by the most delicate balance. In several experiments made in order to ascertain whether, by careful measurement by a micrometer, it is possible to obtain the

* *Baros*, weight—*Opticus*, sight—the weight or an object ascertained by inspection.

weight of a minute crystal, the specific gravity of which is known, I obtained the following results:—So long as the crystal has a definite form, no difficulty is experienced; but when a drop of a solution is allowed to slowly evaporate, or when a crystalline-compound is formed by precipitation, the great practical difficulty is found to be the liability of only a *part* of the deposit to be crystalline in most cases, some small portion being deposited either in an amorphous condition, in dots, or in irregular masses. Nevertheless, in not a few cases, the expert can obtain a fairly accurate weight, if he only give the necessary time to the measurements of the separate and single crystals which compose the unweighable film or deposit.

The details of the operation are as follows:—A micrometer eye-piece is used, and the value of each division of the eye-piece determined in the way recommended in vol. i., “Foods,” p. 73. The eye-piece of the microscope should be made to turn with great ease, and the dimensions of each crystal taken by adjusting the micrometer to its chief edges. What, and how many, measurements will be required, depends, of course, upon the form of the crystal—thus, for example, a cubical crystal will only require one side measured, and that side, multiplied three times into itself, gives the solidity or cubical content. The solidity of a rectangular crystal is obtained by multiplying the length or breadth and depth together. The solidity of a triangular prism is obtained by multiplying the area of the base (see Fig. 14) A B E by the length A B. In such a case, a measurement of A D would also give A E and E D, for these sides are equal; supposing that A B measured 20 micrometer divisions, and A D measured 2.6, the area of the base A E D is then, according to ordinary rules,* $\sqrt{3.75 \times 1.25 \times 1.25 \times 1.25} = 2.7063$, and the solidity is $2.7063 \times 20 = 54.126$, this number requiring to be translated into millimetres.

To obtain the necessary dimensions of not a few crystals, may require a careful measurement of one or more angles, and the application of the rules of trigonometry. A considerable acquaintance with the geometric forms of crystals, as laid down in works on crystallography, is essential to success if the baroscopic method is largely applied.

* The area of a triangle, the sides having been given, is found by subtracting from half the sum of the three sides, each side severally; half the sum of the three remainders are continually multiplied together, and the square root of the last product is the area of the triangle.



Fig. 14.

II. LIQUID VOLATILE ALKALOIDS.

THE ALKALOIDS OF HEMLOCK—NICOTINE—PITURIE—SPARTEINE.

1. THE ALKALOIDS OF HEMLOCK (CONIUM.)

The *conium maculatum*, or spotted hemlock, is a rather common umbelliferous plant, growing in waste places, and flowering from about the beginning of June to August. The stem is from three to five feet high, smooth, branched, and spotted with purple; the leaflets of the partial involucres are unilateral, ovate, lanceolate, with an attenuate point shorter than the umbels; the seeds are destitute of vittæ, and have five prominent crenate wavy ridges. The whole plant is foetid and poisonous. Conium owes its active properties to a volatile liquid alkaloid, *Coniine*, united with a crystalline alkaloid, *Conhydrine*.

Coniine, conia, conicine ($C_8H_{15}N$)—specific gravity, .886 to .381, boiling point, $163\cdot5^{\circ}$ —is a clear, oily fluid, possessing a peculiarly unpleasant, mousey odour. One part is soluble in 100 parts of water, in 6 parts of ether, and in almost all proportions of amyl alcohol, chloroform, and benzene. It readily volatilises, and, provided air is excluded, may be distilled unchanged. It ignites easily, and burns with a smoky flame. It acts as a strong base, precipitating the oxides of metals and alkaline earths from their solutions, and it coagulates albumen. Coniine forms salts with hydrochloric acid ($C_8H_{15}N \cdot HCl$), phosphoric acid, iodic acid, and oxalic acid, which are in well-marked crystals. The sulphate, nitrate, acetate, and tartrate are, on the other hand, non-crystalline.

If coniine is oxidised with nitric acid, or bichromate of potash, and diluted sulphuric acid, butyric acid is formed; and since the latter has an unmistakable odour, and other characteristic properties, it has been proposed as a test for coniine. This may be conveniently performed thus:—A crystal of potassic bichromate is put at the bottom of a test-tube, and some diluted sulphuric acid with a drop of the supposed coniine added. On heating, the butyric acid reveals itself by its odour, and can be distilled into baryta water, the butyrate of baryta being subsequently separated in the usual way, and decomposed by sulphuric acid, &c.

Another test for coniine is the following:—If dropped into a solution of alloxan, the latter is coloured after a few minutes an intense purple-red, and white needle-shaped crystals are separated, which dissolve in cold potash-lye into a beautiful purple-blue, and emit an odour of the base.* Dry hydrochloric acid gives a purple-red, then an indigo-

* Schwarzenbach. *Vierteljahrsschr. f. Pract. Pharm.*, viij., 170.

blue colour, with coniine; but if the acid is not dry, there is formed a bluish-green crystalline mass. This test, however, is of little value to the toxicologist, the pure substance alone responding with any definite result.

The ordinary precipitating agents, according to Dragendorff, act as follows:—

Potass. bismuth iodide.

1 : 2000, a strong orange precipitate.

1 : 3000. The drop of the reagent is surrounded with a muddy border.

1 : 4000. The drop of the reagent is surrounded with a muddy border.

1 : 5000, still perceptible.

1 : 6000. The last limit of the reaction.

Phosphomolybcid acid gives a strong yellow precipitate; limit, 1 : 5000.

Potass. mercuric iodide gives a cheesy precipitate; limit, 1 : 1000 in neutral, 1 : 800 in acid, solutions.

Potass. cadmic iodide gives an amorphous precipitate, 1 : 300. The precipitate is soluble in excess of the precipitant. (Nicotine, under similar circumstances, gives a crystalline precipitate.)

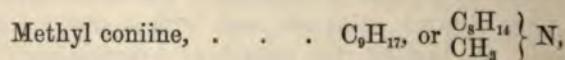
Of all these tests the most satisfactory are—

(1.) The formation of microscopic needles of hydrochlorate of coniine, doubly refracting light, and evolving a mousey odour when breathed upon.

(2.) The formation of butyric acid in oxidation.

(3.) The reaction with alloxan.

Most of the coniine of commerce contains—



a substance which can be formed artificially by warming coniine with methyl iodide, treating the mixture with soda-lye, and distilling. It seems probable that the base which MM. Michael and Gundelach * have recently obtained, by the reaction of butyldene chloride and methylamine, is identical with methylconiine. It is very similar to coniine in appearance; and Drs. Crum Brown and Fraser have established the fact that its toxic action is both qualitatively and quantitatively equal to

* *Ber. der Deutsch. Chem. Ges.*, xiv.

that of coniine. Ethyl coniine and methyl coniine are also similar in action to coniine.

Conhydrine ($C_8H_{17}NO$) is frequently present in coniine, from which it may be separated by cooling down to 5° , filtering through glass wool, and purifying the crystals on the filter by petroleum ether, in which fluid conhydrine does not readily dissolve. Conhydrine forms colourless glittering crystals, which melt about 120.6° , the resulting fluid boiling at 226.3° ; at higher temperatures it volatilises without residue. It dissolves somewhat in water, and easily in alcohol and ether; the solution is strongly alkaline.

Conhydrine is a poison similar to, but not quite so powerful as, coniine. It has little medico-legal interest. Wertheim's experiments appear to show that for every 100 of coniine, hemlock contains only 5.7 of conhydrine.*

Pharmaceutical Preparations.—The percentage of coniine in the plant itself, and in pharmaceutical preparations, can be approximately determined by distilling the coniine over, in a partial vacuum,† and titrating the distillate with Mayer's reagent, each cc.—about .00416 grm. of coniine. It appears to be necessary to add powdered potassic chloride and a small quantity of diluted sulphuric acid before titrating, or the precipitate does not separate. In any case, the end of the reaction is difficult to observe.‡

The fresh plant is said to contain from about .04 to .09 per cent., and the fruit about 7 per cent. of coniine.

The officinal preparations are—the leaves, the fruit, a tincture of the fruit, an extract of the leaves, the juice of the leaves (*Succus conii*), a compound hemlock pill (composed of extract of hemlock, ipecacuanha, and treacle), an inhalation of coniine (*Vapor conii*), and a poultice (*Cataplasma conii*), made with the leaves.

Statistics of Coniine Poisoning.—F. A. Falck§ has been able to collect seventeen cases of death recorded in medical literature, up to the year 1880, from either coniine or hemlock. Two of these cases were criminal

* By the reaction between butylic aldehyde and alcoholic ammonia, Schiff has prepared an isomeride of coniine—paraconiine. It is a nitrile base, while coniine is an imine base; it is poisonous, and similar in its action to coniine.

† This is easily effected by uniting a flask containing the alkaloid fluid, airtight, with a Liebig's condenser and a receiver, the latter being connected with Bunsen's water-pump, or one of the numerous exhausting apparatuses now in use in every laboratory.

‡ Dragendorff, *Die Chemische Werthbestimmung einiger starkwirkender Drogen*. St. Petersb., 1874.

§ *Prakt. Toxicologie*, p. 273.

(murders), one suicidal, two cases in which coniine had been used medicinally (in one instance the extract had been applied to a cancerous breast ; in the other, death was produced from the injection of an infusion of hemlock leaves). The remaining twelve were cases in which the root, leaves, or other portions of the plant had been ignorantly or accidentally eaten.

Effects on Animals.—It destroys all forms of animal life. I have recently made an investigation as to its action on the common blow-fly. Droplets of coniine were applied to various parts of blow-flies, which were then placed under glass shades. The symptoms began within a minute by signs of external irritation, there were rapid motions of the wings, and quick and aimless movements of the legs. Torpor set in speedily, the buzz soon ceased, and the insects lay on their sides, motionless, but for occasional twitching of the legs. The wings, as a rule, become completely paralysed before the legs, and death occurred at a rather variable time, from ten minutes to two hours. If placed in a current of air in the sun, a fly completely under the influence of coniine may recover. Coniine causes in frogs universal paralysis (which is not preceded by convulsions) and speedy death. Dragendorff experimented on the action of coniine when given to five cats, the quantities used being '5 to '05 grm. The symptoms came on almost immediately, but with the smaller dose given to a large cat, no effect was witnessed until twenty-five minutes afterwards : this was the longest interval. One of the earliest phenomena was dilatation of the pupil, followed by weakness of the limbs passing into paralysis, the hinder legs being affected prior to the fore. The respiration became troubled, and the frequency of the breathing diminished ; the heart in each case acted irregularly, and the sensation generally was blunted ; death was preceded by convulsions. In the cases in which the larger dose of '4 to '5 grm. was administered, death took place within the hour, one animal dying in eight minutes, a second in eighteen minutes, a third in twenty minutes, and a fourth in fifty-eight minutes. With the smaller dose of '051 grm. given to a large cat, death did not take place until eight hours and forty-seven minutes after administration.

Effects on Man.—In a case recorded by Bennet,* and quoted in most works on forensic medicine, the symptoms were those of general muscular weakness deepening into paralysis. The patient had eaten hemlock in mistake for parsley ; in about twenty minutes he experienced weakness in the lower extremities, and staggered in walking like a drunken man ; within two hours there was perfect paralysis of both upper and lower extremities, and he died in three and a quarter hours. In another case, related by Taylor, the symptoms were also mainly those of paralysis,

* *Edin. Med. and Surg. Journ.*, July, 1845, p. 169.

and in other instances, stupor, coma, and slight convulsions have been noted.

Physiological Action.—It is generally agreed that coniine paralyses, first the ends of the motor nerves, afterwards their trunks, and lastly, the motor centre itself. At a later period the sensory nerves participate. In the earlier stage the respiration is quickened, the pupils contracted, and the blood-pressure increased; but on the development of paralysis the breathing becomes slowed, the capillaries relaxed, and the blood-pressure sinks. Death takes place from cessation of the respiration, and not primarily from the heart, the heart beating after the breathing has stopped. Coniine is eliminated by the urine, and is also in part separated by the lungs, while a portion is, perhaps, decomposed in the body.

Post-mortem Appearances.—There is nothing characteristic in the appearances after death.

Fatal Dose.—The fatal dose of coniine is not known; in the case of Louise Berger, 10 to 15 drops appear to have caused death in a few minutes. The auto-experiments of Dworzak, Heinrich, and Dillaberger, would indicate that one drop may cause unpleasant symptoms. Albers, in the treatment of a woman suffering from cancer of the breast, witnessed convulsions and loss of consciousness from a third dose of 4 mgrms. (·06 grain); and Eulenberg, its full narcotic effects on a child after subcutaneous injection of 1 mgrm. (·015 grain).

Separation of Coniine from Organic Matters or Tissues.—The substances are digested with water, acidulated with H_2SO_4 , at a temperature not exceeding 40° , and then filtered. If the filtrate should be excessive, it must be concentrated; alcohol is then added, the liquid refiltered, and from the filtrate the alcohol separated by distillation.

On cooling, the acid fluid is agitated with benzene, and the latter separated in the usual way. The fluid is now alkalised with ammonia, and shaken up once or twice with its own volume of petroleum ether; the latter is separated and washed with distilled water, and the alkaloid is obtained almost pure. If the petroleum ether leaves no residue, it is certain that the alkaloid was not present in the contents of the stomach or intestine.

The affinity of coniine with ether or chloroform is such, that its solution in either of these fluids, passed through a *dry* filter, scarcely retains a drop of water. In this way it may be conveniently purified, the impurities dissolved by water remaining behind.

In searching for coniine, the stomach, intestines, blood, urine, liver, and lungs, are the parts which should be examined. According to Dragendorff, it has been discovered in the body of a cat six weeks after death.

Great care must be exercised in identifying any volatile alkaloid as

coniine, for the sources of error seem to be numerous. In one case* a volatile coniine, like ptomaine, was separated from a corpse, and thought to be coniine; but Otto found that in its behaviour to platinic chloride, it differed from coniine; it was very poisonous—.07 was fatal to a frog, .44 to a pigeon, in a few minutes. In the seeds of *Lupinus luteus* there is a series of coniine-like substances† but they do not give the characteristic crystals with hydrochloric acid.

2. NICOTINE.

The various species of tobacco found in commerce all contain a liquid, volatile, poisonous alkaloid (*Nicotine*), probably united in the plant with citric and malic acids. There is also present in tobacco an unimportant camphor (*nicotianin*). The general composition of the plant may be gathered from the following table:—

TABLE IX.—FRESH LEAVES OF TOBACCO (POSSELT AND RIENMANN).

Nicotine,	0.060
Concrete volatile oil,	0.010
Bitter extractive,	2.870
Gum with malate of lime,	1.740
Chlorophyl,	0.267
Albumen and gluten,	1.308
Malic acid,	0.510
Lignine and a trace of starch,	4.969
Salts (sulphate, nitrate, and malate of potash, chloride of potassium, phosphate and malate of lime, and malate of ammonia,	0.734
Silica,	0.088
Water,	88.280
	100.836

Quantitative Estimation of Nicotine in Tobacco.—The best process (although not a perfectly accurate one) is the following:—25 grms. of the tobacco are mixed with milk of lime, and allowed to stand until there is no odour of ammonia; the mixture is then exhausted by petroleum ether, the ether shaken up with a slight excess of normal sulphuric acid, and titrated back by baryta water; the sulphate of baryta may be collected and weighed, so as to control the results with regard to the percentage of nicotine in commercial tobacco. Kosutany found from 1.686

* Otto, *Anleitung z. Ausmittlung d. Gifte*, 1875.

† Sievert, *Zeitschrift für Natur. Wissenschaften*.

to 3.738 per cent. in dry tobacco ; Letheby, in six samples, from 1.5 to 3.2 per cent. ; whilst Schlössing gives for Havanna, 2 per cent., Maryland, 2.29 per cent., Kentucky, 6.09 per cent., Virginian, 6.87 per cent., and for French tobacco, quantities varying from 3.22 to 7.96 per cent. Again, Lenoble found in Paraguay tobacco from 1.8 to 6 per cent. ; and Wittstein, in six sorts of tobacco in Germany, 1.54 to 2.72 per cent. We are thus driven to the conclusion that the alkaloid varies within very wide limits, although it is quite possible that the processes of extraction and estimation by these various observers are of unequal value.

Nicotine ($C_{10}H_{14}N_2$), when pure, is an oily, colourless fluid, of 1.0111, specific gravity at 15° .* It evaporates under 100° in white clouds, and boils about 240° , at which temperature it partly distils over unchanged, and is partly decomposed—a brown resinous product remaining. It volatilises with aqueous and amyl alcohol vapour notably, and is not even fixed at -10° . It has a strong alkaline reaction, and rotates a ray of polarised light to the left. Its odour, especially on warming, is strong and unpleasantly like tobacco, and it has a sharp caustic taste. It absorbs water exposed to the air, and dissolves in water in all proportions, partly separating from such solution on the addition of a caustic alkali. The aqueous solution acts in many respects like ammonia, saturating acids fully, and may therefore be in certain cases estimated with accuracy by titration, 49 parts of H_2SO_4 corresponding to 162 of nicotine.

Alcohol and ether dissolve nicotine in every proportion ; if such solutions are distilled, nicotine goes over first. The salts which it forms with hydrochloric, nitric, and phosphoric acids crystallise with difficulty ; tartaric and oxalic acid form white crystalline salts, and the latter, oxalate of nicotine, is soluble in alcohol, a property which distinguishes it from the oxalate of ammonia. The oxalate of nicotine is the best salt from which to regenerate nicotine in a pure state.

Hydrochloride of nicotine is more easily volatilised than the pure base. Nicotine is precipitated by alkalies, &c., also by many oxyhydrates, lead, copper, &c. By the action of light, it is soon coloured yellow and brown, and becomes thick, in which state it leaves, on evaporation, a brown, resinous substance, only partly soluble in petroleum ether.

A very excellent test for nicotine, as confirmatory of others, is the beautiful, long, needle-like crystals obtained by adding to an ethereal solution of nicotine a solution of iodine in ether. The crystals require a few hours to form.

Chlorine gas colours nicotine blood-red or brown ; the product is soluble in alcohol, and separates on evaporation in crystals.

Cyanogen also colours nicotine brown ; the product out of alcohol is

* J. Skalweit, *Ber. der. Deutsch. Chem. Gesell.*, 14, 1809.

not crystalline. Platin chloride throws down a reddish crystalline precipitate, soluble on warming; and gallic acid gives a flocculent precipitate. A drop of nicotine poured on dry chromic acid blazes up, and gives out an odour of tobacco camphor; if the ignition does not occur in the cold, it is produced by a gentle heat. It is scarcely possible to confound nicotine with ammonia, by reason of its odour; and, moreover, ammonia may always be excluded by converting the base into the oxalate, and dissolving in absolute alcohol.

On the other hand, a confusion between coniine and nicotine is apt to occur when small quantities only are dealt with. It may, however, be guarded against by the following tests:—

(1.) If coniine be converted into oxalate, the oxalate dissolved in alcohol, and coniine regenerated by distillation (best in *vacuo*) with caustic-lye, and then hydrochloric acid added, a crystalline hydrochlorate of coniine is formed, which double refracts light, and is in needle-shaped or columnar crystals, or dendritic, moss-like forms. The columns afterwards become torn, and little rows of cubical, octahedral, and tetrahedral crystals (often cross or dagger-shaped) grow out of yellow amorphous masses. Crystalline forms of this kind are rare, save in the case of dilute solutions of chloride of ammonium (the presence of the latter is, of course, rendered by the treatment impossible); and nicotine does not give anything similar to this reaction.

(2.) Coniine coagulates albumen; nicotine does not.

(3.) Nicotine yields a characteristic crystalline precipitate with an aqueous solution of mercuric chloride; the similar precipitate of coniine is amorphous.

Effects on Animals.—Nicotine is rapidly fatal to all animal life—from the lowest to the highest forms. That tobacco-smoke is inimical to insect-life is known to everybody; very minute quantities in water kill infusoria. Fish of 30 grms. weight die in a few minutes from a milligram of nicotine; the symptoms observed are rapid movements, then shivering and speedy paralysis, with decreased motion of the gills, and death. With frogs, if doses not too large are employed, there is first great restlessness, then strong tetanic convulsions, and a very peculiar position of the limbs; the respiration after fatal doses soon ceases, but the heart beats even after death. Birds also show tetanic convulsions followed by paralysis and speedy death. The symptoms witnessed in mammals poisoned by nicotine are not essentially dissimilar. With large doses the effect is similar to that of prussic acid—viz., a cry, one or two shuddering convulsions, and death. If the dose is not too large, there is trembling of the limbs, excretion of faeces and urine, a peculiar condition of stupor, a staggering gait, and then the animal falls on its side. The respiration at first quickens, is afterwards slowed, and becomes deeper than natural; the pulse

also, with moderate doses, is first slowed, then rises in frequency, and finally, again falls. Tetanic convulsions soon develop ; during the tetanus the pupils have been noticed to be contracted, but afterwards dilated, the tongue and mouth are livid, and the vessels of the ear dilated. Very characteristic of nicotine poisoning as witnessed in the cat, the rabbit, and the dog, is its peculiarly violent action, for after the administration of from one to two drops, the whole course from the commencement of symptoms to the death may take place in five minutes.

The larger animals, such as the horse, are affected similarly to the smaller domestic animals. A veterinary surgeon, Mr. John Howard, of Woolwich,* has recorded a case in which a horse suffered from the most violent symptoms of nicotine-poisoning, after an application to his skin of a strong decoction of tobacco. The symptoms were trembling, particularly at the posterior part of the shoulders, as well as at the flanks, and both fore and hind extremities ; the superficial muscles were generally relaxed and felt flabby ; and the pupils were widely dilated. There was also violent dyspnoea, the respirations being quick and short, pulse 32 per minute, and extremely feeble, fluttering, and indistinct. When made to walk, the animal appeared to have partly lost the use of its hind limbs, the posterior quarter rolling from side to side in an unsteady manner, the legs crossing each other, knuckling over, and appearing to be seriously threatened with paralysis. The anus was very prominent, the bowels extremely irritable, and tenesmus was present. He passed much flatus, and at intervals of three or four minutes, small quantities of faeces in balls, partly in the liquid state, and coated with slimy mucous. There was a staring, giddy, intoxicated appearance about the head and eyes, the visible mucous membrane being of a dark-red colour. A great tendency to collapse was evident, but by treatment with cold douches and exposure to the open air, the horse recovered.

In a case occurring in 1863, in which six horses ate oats which had been kept in a granary with tobacco, the symptoms were mainly those of narcosis, and the animals died.†

Effects on Man.—Poisoning by the pure alkaloid nicotine is so rare that, up to the present, only three cases are on record. The first of these is ever memorable in the history of toxicology, being the first instance in which a pure alkaloid had been criminally used. The detection of the poison exercised the attention of the celebrated chemist Stas. I allude, of course, to the poisoning of M. Fougnies by Count Bocarmé and his wife. For the unabridged narrative of this interesting case, the reader may consult Tardieu's *Etude Médico-Légale sur l'Empoisonnement*.

* *Veter. Journal*, vol. iii.

† *Annales Vétérinaires*. Bruxelles, 1868.

Bocarmé actually studied chemistry in order to prepare the aikaloid himself, and after having succeeded in enticing his victim to the chateau of Bitremont, administered the poison forcibly. It acted immediately, and death took place in five minutes. Bocarmé now attempted to hide all trace of the nicotine by pouring strong acetic acid into the mouth and over the body of the deceased. The wickedness and cruelty of the crime were only equalled by the clumsy and unskilful manner of its perpetration. The quantity of nicotine actually used in this case must have been enormous; for Stas separated no less than '4 grm. from the stomach of the victim.

The second known case of nicotine-poisoning was that of a man who took it for the purpose of suicide. The case is related by Taylor. It occurred in June, 1863. The gentleman drank an unknown quantity from a bottle; he stared wildly, fell to the floor, heaving a deep sigh, and died quietly without convulsion. The third case happened at Cherbourg,* where an officer committed suicide by taking nicotine, but how much had been swallowed, and what were the symptoms, are equally unknown, for no one saw him during life.

Poisoning by nicotine, pure and simple, then, is rare. Tobacco-poisoning is very common, and has probably been experienced in a mild degree by every smoker in first acquiring the habit. Nearly all the fatal cases are to be ascribed to accident; but criminal cases are not unknown. Christison relates an instance in which tobacco in the form of snuff was put into whisky for the purpose of robbery. In 1854 a man was accused of attempting to poison his wife by putting snuff into her ale, but acquitted. In another case, the father of a child, ten weeks old, killed the infant by putting tobacco into its mouth. He defended himself by saying that it was applied to make the child sleep.

In October, 1855,† a drunken sailor swallowed (perhaps for the purpose of suicide) his quid of tobacco, containing from about half an ounce to an ounce. He had it some time in his mouth, and in half an hour suffered from frightful tetanic convulsions. There was also diarrhoea; the pupils were dilated widely; the heart's action became irregular; and towards the end the pupils again contracted. He died in a sort of syncope, seven hours after swallowing the tobacco.

In 1829 a curious instance of poisoning occurred in the case of two girls, eighteen years of age, who suffered from severe symptoms of tobacco poisoning after drinking some coffee. They recovered; and it was found that tobacco had been mixed with the coffee-berries, and both ground up together.‡

* *Ann. d'Hygiène*, 1861, x., p. 404.

† *Edin. Med. Journ.*, 1855.

‡ *Barkhausen, Pr. Ver. Ztg.*, v., 17, p. 83, 1838.

Accidents have occurred from children playing with old pipes. In 1877 * a child, aged three, used for an hour an old tobacco-pipe, and blew soap-bubbles with it. Symptoms of poisoning soon showed themselves, and the child died in three days.

Tobacco-juice, as expressed or distilled by the heat developed in the usual method of smoking is very poisonous. Sonnenschein relates the case of a drunken student, who was given a dram to drink, into which his fellows had poured the juice from their pipes. The result was fatal. Death from smoking is not unknown.† Helwig saw death follow in the case of two brothers, who smoked seventeen and eighteen German pipefuls of tobacco. Marshall Hall ‡ records the case of a young man, nineteen years of

* *Edin. Med. and Surg. Journ.*, xii., 1816.

† The question as to whether there is any nicotine in tobacco-smoke cannot be considered settled; but it is probable that all the poisonous symptoms produced are referable to the pyridene-bases of the general formula ($C_nH_{2n-5}N$). Vohl and Eulenberg (*Arch. Pharmac.*, 2 *cxlii.*, p. 130) made some very careful experiments on the smoke of strong tobacco, burnt both in pipes and also in cigars. The method adopted was to draw the smoke first through potash, and then through dilute sulphuric acid. The potash absorbed prussic acid, hydric sulphide, formic, acetic, propionic, butyric, valeric, and carbolic acids; while in the acid the bases were fixed, and these were found to consist of the whole series of pyridene bases, from pyridene (C_5H_5N), boil. point 117°, picoline (C_6H_7N), boil. point 133°, lutidine (C_7H_9N), boil. point 154°, upwards. When smoked in pipes, the chief yield was pyridene; when in cigars, collidine ($C_8H_{11}N$); and in general, pipe-smoking was found to produce a greater number of volatile bases. The action of these bases has been investigated by several observers. They all have a special action on the organism, and all show an increase in physiological activity as the series is ascended. The lowest produce merely excitement from irritation of the encephalic nervous centres, and the highest, paralysis of those centres. Death proceeds from gradual failure of the respiratory movements, leading to asphyxia.—(Kendrick and Dewar, *Proc. Roy. Soc.*, xxii., 442; xxiii., 290). The derivatives of the pyridene series are also active. The methiodides strongly excite the brain and paralyse the extremities. A similar but more energetic action is exerted by the ethyl and allyl derivatives; the iodyallyl derivatives are strong poisons. Methylic pyridene carboxylate is almost inactive, but the corresponding ammonium salt gives rise to symptoms resembling epilepsy.—(Ramsay, *Phil. Mag.*, v. 4, 241). One member of the pyridene series β , lutidine has been elaborately investigated by C. Greville Williams and W. H. Waters.—(*Proc. Roy. Soc.*, vol. xxxii., p. 162, 1881). They conclude that it affects the heart profoundly, causing an increase in its tonicity, but the action is almost confined to the ventricles. The auricles are but little affected, and continue to beat after the ventricles have stopped. The rate of the heart's beat is slowed, and the inhibitory power of the vagus arrested. By its action on the nervous cells of the spinal cord, it in the first place lengthens the time of reflex action, and then arrests that function. Finally, they point out that it is antagonistic to strychnine, and may be successfully employed to arrest the action of strychnine on the spinal cord.

‡ *Pharm. Journ.* [3], 377, 1877.

age, who, after learning to smoke for two days attempted two consecutive pipes. He suffered from very serious symptoms, and did not completely recover for several days. Gordon has also recorded severe poisoning from the consecutive smoking of nine cigars. The external application of the leaf may, as already shown in the case of the horse, produce all the effects of the internal administration of nicotine. The old instance, related by Hildebrand, of the illness of a whole squadron of hussars who attempted to smuggle tobacco by concealing the leaf next to their skin, is well known, and is supported by several recent and similar cases. The common practice of the peasantry, in many parts of England, of applying tobacco to stop the bleeding of wounds, and also as a sort of poultice to local swellings, has certainly its dangers. The symptoms—whether nicotine has been taken by absorption through the broken or unbroken skin, by the bowel, by absorption through smoking, or by the expressed juice, or the consumption of the leaf itself—show no very great difference, save in the question of time. Pure nicotine acts with as great a rapidity as prussic acid; while if, so to speak, it is entangled in tobacco, it takes more time to be separated and absorbed; besides which, nicotine, taken in the concentrated condition, is a strong enough base to have slight caustic effects, and thus leaves some local evidences of its presence. In order to investigate the effects of pure nicotine, Dworzak and Heinrich made auto-experiments, beginning with 1 mgrm. This small dose produced unpleasant sensations in the mouth and throat, salivation, and a peculiar feeling spreading from the region of the stomach to the fingers and toes. With 2 mgrms. there were headache, giddiness, numbness, disturbances of vision, torpor, dulness of hearing, and quickened respirations. With 3 to 4 mgrms., in about forty minutes there was a great feeling of faintness, intense depression, weakness, with pallid face and cold extremities, sickness, and purging. One experimenter had shivering of the extremities and cramps of the muscles of the back, with difficult breathing. The second suffered from muscular weakness, faintness, fits of shivering, and creeping sensations about the arms. In two or three hours the severer effects passed away, but recovery was not complete for two or three days. It is therefore evident, from these experiments and from other cases, that excessive muscular prostration, difficult breathing, tetanic cramps, diarrhoea, and vomiting, with irregular pulse, represent both tobacco and nicotine poisoning. The rapidly-fatal result of pure nicotine has been already mentioned; but with tobacco-poisoning the case may terminate lethally in eighteen minutes. This interval is usually short, and with children it is commonly about an hour and a half, although, in the case previously mentioned, death did not take place for two days.

Physiological Action.—Nicotine is absorbed into the blood and ex-

creted unchanged, in part by the kidneys and in part by the saliva (*Dra-
gendorff*). According to the researches of Rosenthal and Krocker,* nicotine acts energetically on the brain, at first exciting it, and then lessening its activity ; the spinal marrow is similarly affected. The convulsions appear to have a cerebral origin ; paralysis of the peripheral nerves follows later than that of the nerve centres, whilst muscular irritability is unaffected. The convulsions are not influenced by artificial respiration, and are therefore to be considered as due to the direct influence of the alkaloid on the nervous system. Nicotine has a striking influence on the respiration, first quickening, then slowing, and lastly arresting the respiratory movements : section of the vagus is without influence on this action. The cause of death is evidently due to the rapid numbing and paralysis of the respiratory centre. Death never follows from heart-paralysis, although nicotine powerfully influences the heart's action, small doses exciting the terminations of the vagus in the heart, and causing a slowing of the beats. Large doses paralyse both the controlling and exciting nerve-centres of the heart ; the heart then beats fast, irregularly, and weakly. The blood-vessels are first narrowed, then dilated, and, as a consequence, the blood-pressure first rises, then falls. Nicotine has a special action on the intestines. As O. Nasse † has shown, there is a strong contraction of the whole tract, especially of the small intestine, the lumen of which may be, through a continuous tetanus, rendered very small. This is ascribed to the peripheral excitation of the intestinal nerves and the ganglia. The uterus is also excited to strong contraction by nicotine ; the secretions of the bile and saliva are increased.

Fatal Dose.—It is not possible to state precisely what is the least fatal dose of nicotine, but probably 6 mgrms. would cause very dangerous symptoms in an adult.

Post-mortem Appearances.—There seem to be no appearances so distinctive as to be justly ascribed to nicotine or tobacco poisoning and no other.

A more or less fluid condition of the blood, and, generally, the signs of death by the lungs, are those most frequently found. In tobacco-poisoning, when the leaves themselves have been swallowed, there may be some inflammatory redness of the stomach and intestine.

Separation of Nicotine from Organic Matters, &c.—The process for the isolation of nicotine is precisely that used for coniine (see p. 241). It appears that it is unaltered by putrefaction, and may be separated and recognised by appropriate means a long time after death. Orfila detected it in an animal two or three months after death ; Melsens discovered the

* *Ueber die Wirkung des Nicotines auf den Thierischen Organismus*, Berlin, 1868.

† *Beiträge zur Physiologie der Darmbewegung*. Leipsic, 1866.

alkaloid unmistakably in the tongues of two dogs, which had been buried in a vessel filled with earth for seven years; and it has been found, by several experiments, in animals buried for shorter periods. Nicotine should always be looked for in the tongue and mucous membrane of the mouth, as well as in the usual viscera. The case may be much complicated if the person supposed to be poisoned should have been a smoker; for the defence would naturally be that there had been either excessive smoking or chewing, or even swallowing accidentally a quid of tobacco.* A ptomaine has been discovered similar to nicotine (see index, "Ptomaines.") Wolkenhaar separated also an alkaloid not unlike nicotine from the corpse of a woman addicted to intemperate habits; but this base was not poisonous, nor did it give any crystals when an ethereal solution was added to an ether solution of iodine. It will be well always to support the chemical evidence by tests on animal life, since the intensely poisonous action of nicotine seems not to be shared by the nicotine-like ptomaines.

3. PITURIE. †

Piturie (C_6H_8N) is a liquid, nicotine-like alkaloid, obtained from the *Duboisia hopwoodii*, a small shrub or tree belonging to the natural order *solanaceæ*, indigenous in Australia. The natives mix piturie leaves with ashes from some other plant, and chew them. Piturie is obtained by extracting the plant with boiling water acidified with sulphuric acid, concentrating the liquid by evaporation, and then alkalising and distilling with caustic soda, and receiving the distillate in hydrochloric acid. The solution of the hydrochlorate is afterwards alkalised and shaken up with ether, which readily dissolves out the piturie. The ether solution of piturie is evaporated to dryness in a current of hydrogen, and the crude piturie purified by distillation in hydrogen, or by changing it into its salts, and again recovering, &c. It is clear and colourless when pure and fresh, but becomes yellow or brown when exposed to air and light. It boils and distils at 243° to 244° . It is soluble in all proportions in alcohol, water, and ether; its taste is acrid and pungent; it is volatile at ordinary temperatures, causing white fumes with hydrochloric acid; it is very irritating to the mucous membranes, having a smell like nicotine at first, and then, when it becomes browner, like pyridine. It forms salts with acids, but the acetate, sulphate, and hydrochlorate are varnish-like films having no trace of crystallisation: the oxalate is a crystalline salt. Piturie gives precipitates with mercuric chloride, cupric sulphate, gold chloride, mercur-potassic iodide, tannin, and an alcoholic solution of iodine. If an ethereal solution of iodine is added to an ethereal solution of piturie, a precipitate of yellowish-red needles, readily soluble in alcohol, is deposited. The iodine compound melts at 110° , while the iodine compound of nicotine melts at 100° . Piturie is distinguished from

* In an experiment of Dragendorff's, nicotine is said to have been detected in 35 grms. of the saliva of a person who had half an hour previously smoked a cigar.

† See "The Alkaloid from Piturie," by Prof. Leversidge. *Chem. News*, March 18 and 25, 1881.

coniine by its aqueous solution not becoming turbid either on heating or on the addition of chlorine water; it differs from picoline in specific gravity, picoline being .9613 specific gravity at 0°, and piturie sinking in water; it differs from aniline by not being coloured by chlorinated lime. From nicotine it has several distinguishing marks, one of the best being that it does not change colour on warming with hydrochloric acid and the addition to the mixture afterwards of a little nitric acid. The physiological action seems to be but little different from that of nicotine. It is, of course, poisonous, but as yet has no forensic importance.

4. SPARTEINE.

In 1851 Stenhouse* separated a poisonous volatile alkaloid from *Spartium scoparium*, the common broom, to which he gave the name of sparteine. At the same time a crystalline non-poisonous substance, *scoparin*, was discovered.

Sparteine is separated from the plant by extraction with sulphuric acid holding water, and then alkalisng the acid solution and distilling; it has the formula (C₁₅H₂₈N), and belongs to the class of tertiary diamines. It is a clear, thick, oily substance, scarcely soluble in water, to which it imparts a strong alkaline reaction; it boils at 288°. Sparteine neutralises acids fully, but the oxalate is the only one which can be readily obtained in crystals. It forms crystalline salts with platinic chloride, with gold chloride, with mercuric chloride, and with zinc chloride. The picrate is an especially beautiful salt, crystallising in long needles, which, when dried and heated, explode. On sealing sparteine up in a tube with ethyl iodide and alcohol, and heating to 100° for an hour, ethyl sparteine separates in long, needle-like crystals, which are somewhat insoluble in cold alcohol.

Effect on Animals.—A single drop kills a rabbit; but the symptoms are not yet determined. Mitchell describes a numbness leading into stupor and a comatose condition; while, on the other hand, Schroff described tetanic convulsions.

III. THE OPIUM GROUP OF ALKALOIDS.

Opium contains a larger number of basic substances than any plant known. The list reaches at present to 18 or 19 nitrogenised bases, and almost each year there have been additions. Some of these alkaloids exist in very small proportion, and have been little studied. Morphine and narcotine are those which, alone, are toxicologically important. Opium is a gummy mass, consisting of the juice of the incised unripe fruit of the *Papaver somniferum* hardened in the air. The following is a list of the constituents which have been found in opium :

Morphine, C₁₇H₂₁NO₃.

Narcotine, C₂₂H₂₁NO₇.

Narceine, C₂₂H₂₉NO₉.

Codeine, C₁₈H₂₁NO₃.

Thebaine, C₁₉H₂₁NO₃.

Papaverine, C₂₁H₂₁NO₄.

* *Phil. Trans.*, 1851.

Apomorphine, C ₁₇ H ₁₇ NO ₂ .	} By dehydration of Morphine and Codeine respectively.
Apocodeine, C ₁₈ H ₁₉ NO ₂ .	
Pseudomorphine, C ₁₇ H ₁₉ NO ₄ .	Meconidine, C ₂₁ H ₂₃ NO ₄ .
Codamine, C ₂₀ H ₂₃ NO ₄ .	Meconin, C ₁₉ H ₁₉ O ₄ .
Ladanine, C ₂₀ H ₂₅ NO ₄ .	Meconic Acid, C ₉ H ₁₀ O ₇ .
Ladanosine, C ₂₁ H ₂₇ NO ₄ .	Thebolactic Acid.
Protopine, C ₂₀ H ₁₉ NO ₅ .	Fat.
Cryptopine, C ₂₁ H ₂₃ NO ₅ .	Resin.
Lanthopine, C ₂₂ H ₂₅ NO ₄ .	Caoutchouc.
Hydrocotarnine, C ₁₅ H ₁₈ NO ₂ .	Gummy matters—Vegetable Mucus.
Opianine, C ₂₁ H ₂₁ NO ₇ .	Ash, containing the usual constituents.
Cnoscopine, C ₂₄ H ₂₆ N ₂ O ₁₁ .	
Rhceadine, C ₂₀ H ₂₁ NO ₇ .	

The various opiums differ, the one from the other, in the percentages of alkaloids, so that only a very general statement of the mean composition of opium can be made. The following statement may, however, be accepted as fairly representative of these differences:—

	Per cent.
Morphine,	6 to 15
Narcotine	4 to 8
Other Alkaloids,	5 to 2
Meconin,	Under 1
Meconic Acid,	3 to 8
Peculiar Resin and Caoutchouc,	5 to 10
Fat,	1 to 4
Gum and Soluble Humoid Acid Matters,	40 to 50
Insoluble Matters and Mucus,	18 to 20
Ash,	4 to 8
Water,	8 to 30

The general results of the analysis of 12 samples of Turkey opium, purchased by Mr. Bott,* from leading druggists in London, Dublin and Edinburgh, are as follows:

Water.—Highest, 31.2; lowest, 18.4; mean, 22.4 per cent.

Insoluble Residue.—Highest, 47.9; lowest, 25.45; mean, 32.48 per cent.

Aqueous Extract.—Highest, 56.15; lowest, 20.90; mean, 45.90 per cent.

Crude Morphine (containing about $\frac{7}{10}$ of pure morphine).—Highest, 12.30; lowest, 6.76; mean, 9.92 per cent., which equals 12.3 per cent. of the dried drug.

Persian Opium, examined in the same way, varied in crude morphine from 2.1 to 8.5 per cent.; Malwa, from 5.88 to 7.30. In 18 samples of different kinds of opium, the mean percentage of crude morphine

* *Year Book of Pharmacy*, 1876.

was 8.88 per cent. [11 per cent. of the dried opium]. According to Guibourt, Smyrna opium, dried at 100°, yields 11.7 to 21.46 per cent., the mean being 12 to 14 per cent.; Egyptian, from 5.8 to 12 per cent.; Persian, 11.37 per cent. In East Indian Patna opium, for medical use, he found 7.72; in a sample used for smoking, 5.27 per cent.; in Algerian opium, 12.1 per cent.; in French opium, 14.8 to 22.9 per cent.

Action of Solvents on Opium.—The action of various solvents on opium has been more especially studied by several scientists who are engaged in the extraction of the alkaloids.

Water dissolves nearly everything except resin, caoutchouc, and woody fibre. Free morphine would be left insoluble; but it seems always to be combined with meconic and acetic acids. The solubility of free narcotine in water is extremely small.

Alcohol dissolves resin and caoutchouc, and all the alkaloids and their combinations, with meconic acid, &c.

Amylic Alcohol dissolves all the alkaloids, if they are in a free state, and it also takes up a little of the resin.

Ether, Benzene and Carbon Sulphide do not dissolve the resin, and only slightly morphine, if free; but they dissolve the other free alkaloids as well as caoutchouc.

Acids dissolve all the alkaloids and the resin.

Fixed Alkalies, in excess, dissolve in part resin; they also dissolve morphine freely; narcotine remains insoluble.

Lime Water dissolves morphine, but is a solvent for narcotine only in presence of morphine.

Ammonia dissolves only traces of morphine; but narceine and codeine readily. It does not dissolve the other alkaloids, nor does it dissolve the resin.

Assay of Opium.—The following processes may be described:—

(1.) *Prolli's Method.*—Prolli* has published a simple process of opium assay. The opium is exhausted by water, the watery extract evaporated, and the residue dissolved in alcohol of 34 per cent., and diluted, so that every 10 cc. of the alcoholic solution are equivalent to 1 grm. of the opium. 100 measures of the alcoholic solution are shaken with 5 of ether and 1 of ammonia, and the liquid allowed to stand twenty-four hours. The morphine sinks in crystals to the bottom, while the narcotine and other alkaloids are dissolved by the ether, and remain in solution. The crystals may now be collected, and either weighed or titrated with decinormal acid; 1 cc. of decinormal acid equals .0285 anhydrous morphine.

(2.) *Flückiger's Method*, as modified by Mylius,† is very accurate,

* *Pharm. Central-Halle*, 1878, 20.

† *Arch. Pharm.* (3), xv., p. 310.

and is as follows:—15 grms. are carefully dried at 100°, and the water estimated from the loss. The dried opium is powdered, and 8 grms. of the powder extracted by absolute ether to remove wax, narcotine, and colouring-matter. The residue is freed from ether, and digested for twelve hours in a closed flask with 80 cc. of water; the liquid is filtered, and 42.5 grms. of the filtrate (equivalent to 5 grms. of the dried sample) are transferred to a small flask; 17 cc. of ether-alcohol (made by mixing 100 grms. of ether with 120 grms. of alcohol, specific gravity .815) are added, and 1.5 grms. of ammonia of .860 specific gravity. The flask is then closed, shaken, and put on one side for twenty-four hours. The morphine is now brought on to a weighed filter, which can be effected by detaching any crystals sticking to the side of the flask by a glass rod; they can be washed by a few cc. of ether-alcohol, and the filter gently pressed between folds of blotting-paper till free from mother liquor, dried at 100°, and weighed; the results being too low, on account of the slight solubility of morphine in ether-alcohol, .088 grms. of morphine are to be added, and then the results are said to be absolutely correct. The weight may be checked by titration with decinormal acid.

(3.) *Hager's Method* has the merit of being speedy, although the results are not perfectly accurate. 5 grms. of the powdered opium are thoroughly mixed in a mortar with previously slaked lime, and then heated in a flask for an hour with 50 grms. of distilled water at a boiling temperature. The whole is thrown on a small filter, and washed with hot water until the filtrate weighs 80 grms. The filtrate is concentrated in the water-bath to 50 grms., and placed in a conical glass; 1.5 grms. of ether, and 6 drops of good benzene are then added, which hasten the separation of morphine, and hinder the adhesions of crystals to the sides of the glass. The liquid is well stirred, and 3.5 grms. of chloride of ammonium are added. After three hours the morphine is thus precipitated, separated by filtration, and weighed. The precipitate may be purified by washing with ether; some morphine always remains in solution, but it may, as Dragendorff suggests, be recovered by shaking the alkaline solution with amyl alcohol.*

Medicinal and other Preparations of Opium.—The chief mixtures, pills, and other forms, officinal and non-officinal, in which opium may be met with, are as follows:—

* Other methods of opium assay have been published: see Mr. A. B. Prescott's method (*Proceedings of Amer. Pharm. Assoc.*, 1878); Allen (*Commercial Org. Analysis*, vol. ii., p. 473); E. R. Squibb's modification of Flückiger's method (*Pharm. Journ.* (3), xii., p. 724); a rapid mode of opium assay, MM. Portes and Lanjlois (*Journ. de Pharm. et de Chim.*, Nov., 1881), *Year Book of Pharmacy*, 1882.

To the above may be added—(1) *Schacht's Method*.—Five to 10 grms. of dry, finely-powdered opium are digested with sufficient distilled water to make a thin

(1.) OFFICINAL.

*Compound Tincture of Camphor, P. B.**—Opium, camphor, benzoic acid, oil of anise, and proof spirit.

Opium, . . .	41	by weight in 100 by measure.
Benzoic Acid, . .	41	," , , , "
Camphor, . .	31	," , , , "

One grain of opium is contained in half an ounce of the tincture.

Ammoniated Tincture of Opium.—Strong solution of ammonia rectified spirit, opium, oil of anise, saffron, and benzoic acid.

Opium, . .	1·04	parts by weight in 100 by measure.
Benzoic Acid, 1·87	"	" , , , "

One grain of opium in every 96 minims.

pulp. After twenty-four hours the whole is thrown on a weighed filter, and washed until the washings are almost colourless and tasteless. The portion insoluble in water is dried at 100° and weighed; in good opium this should not exceed 40 per cent. The filtrate is evaporated until it is about one-fifth of the weight of the opium taken originally; cooled, filtered, and treated with pure animal charcoal, until the dark-brown colour is changed into a brownish-yellow. The liquid is then refiltered, precipitated with a slight excess of ammonia, allowed to stand in an open vessel until all odour of ammonia disappears, and at the same time frequently stirred, in order that the precipitate may not become crystalline—a form which is always more difficult to purify. The precipitate is now collected on a tared filter, washed, dried, and weighed. With an opium containing 10 per cent. of morphine its weight is usually 14 per cent. A portion of the precipitate is then detached from the filter, weighed, and exhausted, first with ether, and afterwards with boiling alcohol (0·81 specific gravity). Being thus purified from narcotine, and containing a little colouring-matter only, it may now be dried and weighed, and the amount of morphine calculated, on the whole, from the data obtained.

(2.) *Fleury* has proposed a titration by oxalic acid as follows:—2 grms. of the powdered opium are macerated a few hours with 8 cc. of aqueous oxalate of ammonia, brought on a filter, and washed with 5 cc. of water. To the filtrate an equal volume of 80 per cent. alcohol and ammonia to alkaline reaction is added; and, after standing twenty-four hours in a closed flask, it is filtered, and the flask rinsed out with some cc. of 40 per cent. alcohol. The filter with its contents, after drying, is placed in the same flask (which should not be cleansed), a few drops of alcoholic logwood solution are added, with an excess of oxalic acid solution of known strength, the whole being made up to 100 cc. This is divided into two parts, and the excess of acid titrated back with diluted soda-lye. If the oxalic acid solution is of the strength of 4·42 grms. to the litre, every cc. of the oxalic acid solution which has become bound up with morphine, corresponds to 0·02 grms. of morphine.

* The common appellation of this tincture is *Paregoric* or *Paregoric Elixir*.

The Compound Powder of Kino, P. B.

Opium,	5 per cent.
Cinnamon,	20 ,,
Kino,	75 ,,

The Compound Powder of Opium, P. B.

Opium,	10·00 per cent.
Black Pepper,	13·33 ,,
Ginger,	33·33 ,,
Caraway Fruit,	40·00 ,,
Tragacanth,	3·33 ,,

Pill of Lead and Opium, P. B.

Acetate of Lead,	75·0 per cent.
Opium,	12·5 ,,
Confection of Roses,	12·5 ,,

Tincture of Opium (Laudanum).—Opium and proof spirit. One grain of opium in 14·8 min.—that is, about 6·7 parts by weight in 100 by measure.

The amount of opium actually contained in laudanum has recently been investigated by Mr. Woodland,* from fourteen samples purchased from London and provincial chemists. The highest percentage of extract was 5·01, the lowest 3·21, the mean being 4·24; the highest percentage of morphine was 70 per cent., the lowest 32, the mean being 51 per cent. It is, therefore, clear that laudanum is a liquid of very uncertain strength.

Aromatic Powder of Chalk and Opium.—Opium 2·5 per cent., the rest of the constituents being cinnamon, nutmeg, saffron, cloves, cardamoms, and sugar.

Compound Powder of Ipecacuanha (Dover's Powder).

Opium,	10 per cent.
Ipecacuanha,	10 ,,
Sulphate of Potash,	30 ,,

Confection of Opium (Confectio opii) is composed of syrup and compound powder of opium; according to its formula, it contains 24 per cent. of opium by weight.

Extract of Opium contains the solid constituents capable of extraction by water; its strength is about the same as opium itself.

Liquid Extract of Opium has been also recently examined by Mr.

* *Year Book of Pharmacy, 1882*

Woodland : * ten samples yielded as a mean 3.95 per cent. of dry extract, the highest number being 4.92 per cent., the lowest 3.02. The mean percentage of morphine was .28 per cent., the highest amount being .37, and the lowest .19 per cent.

Liniment of Opium is composed of equal parts of laudanum and soap liniment ; it contains about 3.7 per cent. dry opium.

The Compound Soup-pill is made of soap and opium, one part of opium in every five of the mass—i.e., 20 per cent.

Ipecacuanha and Morphine Lozenges, as the last, with the addition of ipecacuanha ; each lozenge contains $\frac{1}{30}$ grain (1.8 mgrms.) morphine hydrochlorate, $\frac{1}{12}$ grain (5.4 mgrms.) ipecacuanha.

Morphia Suppositories are made with hydrychlorate of morphine, benzoated lard, white wax, and oil of theobroma ; each suppository contains $\frac{1}{2}$ grain (32.4 mgrms.) of morphine salt.

Opium Lozenges are composed of opium extract, tincture of tolu, sugar, gum, extract of liquorice, and water. Each lozenge contains one-tenth of a grain (6.4 mgrms.) of extract of opium.

The Ointment of Galls and Opium contains one part of opium in 14.5 parts of the ointment—i.e., opium 6.9 per cent.

Opium Wine, P. B.—Sherry, opium extract, cinnamon, and cloves. About 4.5 of opium extract by weight in 100 parts by measure (22 grains to the ounce).

Solutions of Morphine, both of the acetate and hydrochlorate, P. B., are made with a little free acid, and with rectified spirit. The strength of each is half a grain in each fluid drachm, (.0324 grm. in 3.549), or .91 part by weight in 100 by measure.

Morphia Lozenges are made with the same accessories as opium lozenges, substituting morphine for opium ; each lozenge contains $\frac{1}{30}$ grain of hydrochlorate of morphia (1.8 mgrms.)

Syrup of Poppies.—The ordinary syrup of poppies is sweetened laudanum. It should, however, be what it is described—viz., a syrup of poppy-heads. As such, it is said to contain one grain of extract of opium to the ounce.

(2.) PATENT AND OTHER NON-OFFICINAL PREPARATIONS OF OPIUM.

Godfrey's Cordial is made on rather a large scale, and is variable in strength and composition. It usually contains about 1½ grains of opium in each fluid ounce,† and, as other constituents : sassafras, molasses or treacle, rectified spirit, and various flavouring ingredients, especially

* *Op. cit.*

† If made according to Dr. Paris' formula, 1 1-6 grains in an ounce.

ginger, cloves, and coriander; aniseed and caraways may also be detected.

Grinrod's Remedy for Spasms consists of hydrochlorate of morphine, spirits of sal-volatile, ether, and camphor julap; strength, 1 grain of the hydrochlorate in every 6 ounces.

Lemaurier's Odontalgic Essence is acetate of morphine dissolved in cherry-laurel water; strength, 1 grain to the ounce.

Nepenthe is a preparation very similar to *Liq. Opii sedativ.*, and is of about the same strength as laudanum.*

Black Drop (known also by various names, such as Armstrong's *Black Drop*) is essentially an acetic acid solution of the constituents of opium. It is usually considered to be of four times the strength of laudanum. The wholesale receipt for it is: Laudanum, 1 ounce, and distilled vinegar, 1 quart, digested for a fortnight. The original formula proposed by the Quaker doctor of Durham, Edward Tunstall, is—Opium, sliced, $\frac{1}{2}$ lb.; good verjuice, † 3 pints; and nutmeg, $1\frac{1}{2}$ ounce, boiled down to a syrupy thickness; $\frac{1}{4}$ lb. of sugar and 2 teaspoonfuls of yeast are then added. The whole is set in a warm place for six or eight weeks, after which it is evaporated in the open air until it becomes of the consistence of a syrup. It is lastly decanted and filtered, a little sugar is added, and the liquid made up to 2 pints.

“*Nurse's Drops*” seem to be composed of oil of caraway and laudanum.

Dalby's Carminative—

Carbonate of Magnesia,	40 grains.
Tincture of Castor, and Compound	
Tincture of Cardamoms, of each .	15 drops.
Laudanum,	5 "
Oil of Aniseed,	3 "
Oil of Nutmeg,	2 "
Oil of Peppermint,	1 "
Peppermint Water,	2 fl. ounces.

Dose, from a half to one teaspoonful. Another recipe has no laudanum, but instead syrup of poppies.

Chlorodyne—Brown's chlorodyne is composed of—

Chloroform,	6 drachms.
Chloric Ether,	1 "

* It may be regarded as a purified alcoholic solution of meconate of morphia with a little excess of acid, and of about the same strength as laudanum. (Taylor.)

† Verjuice is the juice of the wild crab.

Tincture of Capsicum,	$\frac{1}{2}$ drachm.
Hydrochlorate of Morphine,	8 grains.
Scheele's Prussic Acid,	12 drops.
Tincture of Indian Hemp,	1 drachm.
Treacle,	1 , ,

Atkinson's Infant Preserver—

Carbonate of Magnesia,	6 drachms.
White Sugar,	2 ounces.
Oil of Aniseed,	20 drops.
Spirit of Sal-volatile,	2½ drachms.
Laudanum,	1 , ,
Syrup of Saffron,	1 ounce.
Caraway Water, to make up	1 pint.

Boerhave's Odontalgic Essence—

Opium,	$\frac{1}{2}$ drachm.
Oil of Cloves,	2 , ,
Powdered Camphor,	5 , ,
Rectified Spirit,	1½ fl. ounce.

Statistics.—In the five years, 1876–1880, 393 males and 250 females died from some form or other of opium poisoning ; 2 only out of the whole number were cases of murder, and in both the victims were infants ; 22·4 per cent. of the female cases and 30·5 of the males were suicidal.

The following table gives a summary of the sex and ages of those poisoned, and the particular form of opiate used :—

TABLE X.—SHOWING THE NUMBER OF DEATHS FROM VARIOUS FORMS OF OPIUM IN ENGLAND, DURING THE FIVE YEARS, 1876-80.

		-5	5-	10-	15-	20-	25-	35-	45-	55-	65-	75-	TOTAL
Opium, . . .	M.	16	3	7	12	12	8	15	8	1	89
	F.	17	..	2	..	2	5	3	10	12	11	3	65
Laudanum and Syrup of Poppies, . . .	M.	45	1	..	2	13	26	39	41	32	23	6	227
	F.	35	8	7	21	21	21	14	10	4	141
Morphia, . . .	M.	1	1	1	9	10	2	3	1	1	29
	F.	2	1	2	3	..	1	9
Chlorodyne, . . .	M.	4	3	..	1	3	7	5	4	6	2	1	36
	F.	3	1	1	3	2	5	2	17
Matthews' Cordial, Godfrey's Cordial, Soothing Syrups, Infant Preservatives, &c. .	M.	17	17
	F.	16	16
Other Opiates, . . .	M.	2	2
	F.	2	2
Total, . . .	M.	85	4	..	7	24	54	66	55	56	33	9	393
	F.	75	2	2	8	10	31	29	36	29	21	7	250

The total cases of death from all poisons in the five years in England were 1581, so that some form of opium poisoning accounted for 40.7 per cent. of the total deaths from all kinds of poison. This is a higher percentage than that found in any other European country. In France, opium or morphine poisoning accounts for about 1 per cent. of the whole; and Denmark, Sweden, Switzerland, Germany, all give very small proportional numbers; arsenic, phosphorus, and the acids taking the place of opiates. The more considerable mortality arises, in great measure, from the pernicious practice—both of the hardworking English mother and of the baby farmer—of giving infants various forms of opium sold under the name of “soothing syrups,” “infants’ friends,” “infants’ preservatives,” “nurse’s drops,” and the like, to allay rest-

lessness, and to keep them during the greater part of their existence asleep. Another fertile cause of accidental poisoning is mistakes in dispensing ; but these mistakes seem to happen more frequently on the Continent than in England. This is in some degree due to the decimal system, which has its dangers as well as its advantages, *e.g.* :—A physician ordered 5 grm. of morphine acetate for a child, but omitted the decimal point, and the apothecary, therefore, gave ten times the dose desired, with fatal effect. Again, morphine hydrochlorate, acetate, and other soluble salts are liable to be mistaken for other white powders, and in this way unfortunate accidents have occurred—accidents that, with proper dispensing arrangements, should be impossible.

Poisoning of Children by Opium.—The drugging of children by opium—sometimes with a view to destroy life, sometimes merely for the sake of the continual narcotism of the infant—is especially rife in India.* A little solid opium is applied to the roof of the mouth, or smeared on the tongue, and some Indian mothers have been known to plaster the nipples with opium, so that the child imbibes it with the milk. Europeans, again and again, have discovered the native nurses administering opiates to the infants under their care, and it is feared that in many cases detection is avoided.

The ignorant use of poppy-tea has frequently caused the death of young children. Thus in 1875 an inquest was held at Chelsea on the body of a little boy, two years and a half old. He had been suffering from whooping-cough and enlargement of the bowels, and poppy-tea was by the advice of a neighbour given to him. Two poppy-heads were used in making a quart of tea, and the boy, after drinking a great portion of it, fell into a deep sleep, and died with all the symptoms of narcotic poisoning.

Doses of Opium and Morphia.—Opium in the solid state is prescribed for adults in quantities not exceeding 3 grains, the usual dose being from 16·2 mgrms. to 64·8 mgrms. ($\frac{1}{4}$ to 1 grain.) The extract of opium is given in exactly the same proportions (special circumstances, such as the habitual use of opium, excepted) ; the dose of all the compounds of opium is mainly regulated by the proportion of opium contained in them.

The dose for children (who bear opium ill) is usually very small ; single drops of laudanum are given to infants at the breast, and the dose cautiously increased according to age. Most practitioners would consider half a grain a very full dose, and in cases, requiring it, would seldom prescribe at first more than $\frac{1}{16}$ to $\frac{1}{4}$ grain.

The dose of solid opium for a horse is from 1·77 grms. to 7·08 grms. ($\frac{1}{4}$ drachm to 2 drachms) ; in extreme cases, however, 4 drachms (14·16 grms.) have been given.

* See Dr. Chever's "Jurisprudence," 3rd Ed., 232 *et seq.*

The dose for large cattle is from 648 to 3,88 grms. (10 to 60 grains); for calves, 648 grm. (10 grains); for dogs it is greatly regulated by the size of the animal, 16.2 to 129.6 mgrms. ($\frac{1}{4}$ grain to 2 grains).

Fatal Dose.—Cases are recorded of infants dying from extremely small doses of opium—*e.g.*, 7, 4.3, and 8.1 mgrms. ($\frac{1}{90}$, $\frac{1}{15}$, and $\frac{1}{6}$ of a grain); but in such instances one cannot help suspecting some mistake. It may, however, be freely conceded that a very small quantity might be fatal to infants, and that 3 mgrms. given to a child under one year would probably develop serious symptoms.

The smallest dose of solid opium known to have proved fatal to adults was equal to 256 mgrms. (4 grains) of crude opium (*Taylor*), and the smallest dose of the tincture (laudanum), 7.0 cc. (2 drachms), (*Taylor*); the latter is, however, as already shown, uncertain in its composition.

A dangerous dose (save under special circumstances) is:—For a horse, 14.17 grms. (4 drachms); for cattle, 7.04 grms. (2 drachms); for a dog of the size and strength of a foxhound, 182 mgrms. (3 grains).

Enormous and otherwise fatal doses may be taken under certain conditions by persons who are not opium eaters. I have seen 13 cgrms. (2 grains) of morphine acetate injected hypodermically in a strong man suffering from rabies, with but little effect. Tetanus, strychnine, convulsions, and excessive pain all decrease the sensibility of the nervous system to opium.

General Method for the Detection of Opium.—It is usually laid down in forensic works that, where poisoning by opium is suspected, it is sufficient to detect the presence of meconic acid in order to establish that of opium. In a case of adult poisoning there is generally substance enough available to obtain one or more alkaloids, and the presence of opium may, without a reasonable doubt, be proved, if meconic acid (as well as either morphine, narcotine, thebaine, or other opium alkaloid) has been detected. Pills containing either solid opium or the tincture, usually betray the presence of the drug by the odour, and in such a case there can be no possible difficulty in isolating morphine and meconic acid, with probably one or two other alkaloids. The method of extraction from organic fluids is the same as before described, but it may, of course, be modified for any special purpose. If opium, or a preparation of opium, be submitted to Dragendorff's process (see p. 212), the following is a sketch of the chief points to be noticed.

If the solution is *acid*.

(1.) *Benzene* mainly extracts *meconin*, which dissolves in sulphuric acid very gradually (in twenty-four to forty-eight hours), with a green colour passing into red. Meconin has no alkaloidal reaction.

(2.) *Amyl alcohol* dissolves small quantities of *meconic acid*, identified by striking a blood-red colour with ferric chloride.

If now the amyl alcohol is removed with the aid of petroleum ether, and the fluid made alkaline by ammonia—

(1.) *Benzene* extracts *narcotine*, *codeine* and *thebaine* On evaporation of the benzene the alkaloidal residue may be dissolved in water, acidified with sulphuric acid, and after filtration, on adding ammonia in excess, *thebaine* and *narcotine* are precipitated, *codeine* remaining in solution. The dried precipitate, if it contain *thebaine*, becomes blood-red when treated with cold concentrated sulphuric acid, while *narcotine* is shown by a violet colour developing gradually when the substance is dissolved in dilute sulphuric acid 1:5, and gently warmed. The *codeine* in the ammoniacal solution can be recovered by shaking up with benzene, and recognised by the red colour which the solid substance gives when treated with a little sugar and sulphuric acid.

(2.) *Chloroform* especially dissolves the *narcotine*, which, on evaporation of the chloroform, may be identified by its general characters, and by its solution in Fröhde's reagent becoming a beautiful blue colour. Small quantities of morphine may be extracted with *codeine*.

(3.) *Amyl alcohol* extracts from the alkaline solution morphine, identified by its physical characters, by its forming a crystalline precipitate with iodine and hydriodic acid, and the reaction with iodic acid to be described.

Morphine ($C_{17}H_{19}NO_3 + H_2O$).—Morphine occurs in commerce as a white powder, usually in the form of more or less perfect six-sided prisms, but sometimes in that of white silky needles. When heated in the subliming cell (described at p. 229), faint nebulæ, resolved by high microscopic powers into minute dots, appear on the upper disc at 150° . As the temperature is raised, the spots become coarser, and at 188° distinct crystals may be obtained, the best being formed at nearly 200° , at which temperature morphine begins distinctly to brown, melt, and carbonise. At temperatures below 188° , instead of minute dots, the sublimate may consist of white circular spots or foliated patterns. One part of morphine, according to P. Chastaing, is soluble at a temperature of 3° in 33,333 parts of water; at 22° , in 4,545 parts; at 42° , 4,280; and at 100° , 4,562. It is scarcely soluble in ether or benzene. Absolute alcohol, according to Pettenkofer, dissolves in the cold one-fortieth of its weight, boiling, one-thirtieth. Amyl alcohol, in the cold, dissolves one-fourth per cent., and still more if the alkaloid be thrown out of an aqueous acid solution by ammonia in the presence of amyl alcohol; for under such circumstances the morphine has no time to become crystalline. According to Schlimpert, 1 part of morphine requires 60 of chloroform for solution; according to Pettenkofer, 175.

Morphine is easily soluble in dilute acids, as well as in solutions of the caustic alkalies and alkaline earths; carbonated alkalies and chloride of ammonium also dissolve small quantities. The acid watery, and the alcoholic solutions, turn the plane of polarisation to the left; for sulphuric, nitric, and hydrochloric acids $[\alpha]_r = 89.8^\circ$; in alkaline solution the polarisation is less, $[\alpha]_r = 45.22^\circ$. It is alkaline in reaction, neutralising acids fully; and, in fact, a convenient method of titrating morphine is by the use of a centinormal sulphuric acid—each cc. equals 2.85 mgrms. of anhydrous morphine.

The salts of morphine are for the most part crystalline, and are all bitter, neutral, and poisonous. They are insoluble in amylic alcohol, ether, chloroform, benzene, or petroleum ether.

Morphine Meconate is one of the most soluble of the morphine salts; it is freely soluble in water. Of all salts, this is most suitable for subcutaneous injection; it is the form in which the alkaloid exists in opium.

Morphine Hydrocolorate ($C_{17}H_{19}NO_3HCl$) crystallises in silky fibres; it is readily soluble in alcohol, and is soluble in cold, more freely in boiling water. The purest morphine hydrochlorate is colourless, but that which is most frequently met with in commerce is fawn or buff-coloured.

Morphine Acetate is a crystallisable salt, soluble in water or alcohol; it is in part decomposed by boiling the aqueous solution, some of the acetic acid escaping.

Morphine Tartrates. — These are readily soluble salts, and it is important to note that the morphine might escape detection, if the expert trusted alone to the usual test of an alkaloidal salt giving a precipitate when the solution is alkalised by the fixed or volatile alkalies; for the tartrates of morphine do not give this reaction, nor do they give any precipitate with calcic chloride. By adding a solution of potassium acetate in spirit, and also alcohol and a little acetic acid to the concentrated solution, the tartrate is decomposed, and acid tartrate of potassium is precipitated in the insoluble form; the morphine in the form of acetate remains in solution, and then gives the usual reactions.

The solubility of morphine salts in water and alcohol has been recently investigated by Mr. J. U. Lloyd. His results are as follows:—

Morphine Acetate.

11.70 parts of water by weight at 15.0° dissolve 1 part of morphine acetate.

61.5 parts of water by weight at 100° dissolve 1 part of morphine acetate.

68.30 parts of alcohol by weight (·820 specific gravity) at 15.0° dissolve 1 part of morphine acetate.

13.30 parts of alcohol by weight (·820 specific gravity) at 100° dissolve 1 part of morphine acetate.

Morphine Hydrochlorate.

23.40 parts of water dissolve at 15° 1 morphine hydrochlorate.
 ·51 part of water dissolves at 100° 1 morphine hydrochlorate.
 62.70 parts of alcohol (·820 specific gravity) dissolve at 15° 1 morphine hydrochlorate.
 30.80 parts of alcohol (·820 specific gravity) dissolve at 100° 1 morphine hydrochlorate.

Morphine Sulphate.

21.60 parts of water at 15° dissolve 1 morphine sulphate.
 ·75 part of water at 100° dissolves 1 morphine sulphate.
 701.5 parts of alcohol (·820) at 150° dissolve 1 morphine sulphate.
 144.00 parts of alcohol (·820) at 100° dissolve one morphine sulphate.

Tests for Morphine and its Compounds.—There are two chief tests for morphine, or morphine salts. If both these reactions are obtained, there can be no reasonable doubt of the presence of the alkaloid. Objections, more or less valid, may be made to either test taken alone, but together they are conclusive. These are a crystalline compound, with iodine dissolved in hydriodic acid, and what is known as the “iodic acid test.”

(1.) *Production of Morphine Hydriodide.*—The precipitate with iodised hydriodic acid is formed in extremely dilute solutions, and if to a neutral solution no precipitate occurs, it may be confidently asserted that morphine is not present. Papaverine and codeine also give a crystalline precipitate with the same reagent, but the crystals are different in form. Hydriodide of morphine is dark-red in colour; the crystals are either free or collect in little radial groups, very definite in form, and well suited for “*baroptic*” estimation (see p. 235). Their specific gravity is 1.97, every 136.3 of morphine hydriodide equals 100 of morphine crystallised with 1 atom of water.

(2.) *Iodic Acid Test.*—The substance supposed to be morphine is converted into a soluble salt by adding to acid reaction a few drops of hydrochloric acid, and then evaporating to dryness. The salt thus obtained is dissolved in as little water as possible—this, as in toxicological researches only small quantities are recovered, will probably be but a few drops. A little of the solution is now mixed with a very small quantity of starch-paste, and evaporated to dryness at a gentle heat in a porcelain dish. After cooling, a drop of a solution of one part of iodic acid in 15

of water is added to the dry residue ; and if even the $\frac{1}{2000}$ of a grain of morphine be present, a blue-colour will be developed.

Another way of working the iodic acid test is to add the iodic acid solution to the liquid in which morphine is supposed to be dissolved, and then shake the liquid up with a few drops of carbon disulphide. If morphine be present, the carbon disulphide floats to the top distinctly coloured pink. Other substances, however, also set free iodine from iodic acid, and it has, therefore, been proposed to distinguish morphine from these by the after addition of ammonia. If ammonia is added to the solution, which has been shaken up with carbon disulphide, the pink or red colour of the carbon disulphide is deepened, if morphine was present ; on the contrary, if morphine was *not* present, it is either discharged or much weakened.

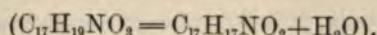
Other Reactions.—There are some very interesting reactions besides the two characteristic tests just mentioned. If a saturated solution of chloride of zinc be added to a little solid morphine, and heated over the water-bath for from fifteen minutes to half-an-hour, the liquid develops a beautiful and persistent green colour. This would be an excellent test for morphine were it not for the fact that the colour is produced with only *pure* morphine. For example, I was unable to get the reaction from morphine in very well-formed crystals precipitated from ordinary laudanum by ammonia, the least trace of resinous or colouring matter seriously interfering. By the action of nitric acid on morphine, the liquid becomes orange-red, and an acid product of the formula $C_{10}H_9NO_3$ is produced, which, when heated in a closed tube with water at 100° , yields trinitro-phenol or picric acid. This interesting reaction points very decidedly to the phenolic character of morphine. On adding a drop of sulphuric acid to solid morphine in the cold, the morphine solution becomes of a faint pink ; on gently warming and continuing the heat until the acid begins to volatilise, the colour changes through a series of brownish and indefinite hues up to black. On cooling and treating the black spot with water, a green solution is obtained, agreeing in hue with the same green produced by chloride of zinc. Vidali* has recently proposed the following test :—Morphine is dissolved in strong sulphuric acid, and a little arsenate of sodium is added ; on gently warming, a passing blue colour develops ; on raising the temperature higher, the liquid changes into green, then into blue, and finally again into green. Codeine acts very similarly. The following test originated with Siebold (*American Journal of Pharmacy*, 1873, p. 544) :—The supposed morphine is heated gently with a few drops of concentrated sulphuric acid and a little pure potassic perchlorate. If

* D. Vidali, *Bull. Farmaceut.*, Milano, 1881, p. 197. D. E. Dott, *Year Book of Pharmacy*, 1882.

morphine be present the liquid immediately takes a pronounced brown colour—a reaction said to be peculiar to morphine, and to succeed with $\frac{1}{10}$ of a mgrm. In order to obtain absolutely pure perchlorate, potassic perchlorate is heated with hydrochloric acid so long as it disengages chlorine; it is then washed with distilled water, dried, and preserved for use. There is also a test known as "Pellagri's;" it depends on the production of apomorphine. The suspected alkaloid is dissolved in a little strong hydrochloric acid, and then a drop of concentrated sulphuric acid is added, and the mixture heated for a little time from 100° to 120° , until it assumes a purple-black colour. It is now cooled, some hydrochloric acid again added, and the mixture neutralised with sodic carbonate. If morphine be present, on the addition of iodine in hydriodic acid, a cherry-red colour is produced, passing into green. Morphine and codeine are believed alone to give this reaction.

E. Grimaux* has succeeded in transforming morphine into codeine. When 1 molecule of morphine is dissolved in alcohol containing 1 molecule of sodium hydroxide, and 2 vols. of methyl iodide are added, and the mixture gently heated, a violent reaction sets in and the main product is codeine methiodide ($C_{17}H_{18}NO_2OCH$, MeI). If only half the quantity of methyl iodide is added, then free codeine is in small quantity produced; if ethyl iodide be substituted for methyl, a new base is formed homologous with codeine—Grimaux considering morphine analogous to phenol—therefore codeine would seem to be the methyl ether of morphine. If morphine is heated with iodide of methyl and absolute alcohol in a closed tube for half an hour at 100° , methyl iodide of morphine is obtained in colourless, glittering, quadratic crystals, easily soluble in water ($C_{17}H_{19}NO_2MeI + H_2O$); similarly the ethyl iodide compound can be produced.

If morphine is heated for from two to three hours in a closed tube with dilute hydrochloric acid, water is eliminated—



and the hydrochlorate of apomorphine is produced.

If concentrated sulphuric acid be digested on morphine for twelve to fifteen hours (or heated for half an hour at 100°), on adding to the cooled violet-coloured solution either a crystal of nitrate of potash or of chlorate of potash, or a drop of dilute nitric acid, a beautiful violet-blue colour is produced, which passes gradually into a dark blood-red. $\frac{1}{100}$ of a mgrm. will respond distinctly to this test. Fröhde's reagent strikes with morphine a beautiful violet colour, passing from blue into dirty green, and

* *Compt. Rend.*, 92, pp. 1140-1143 and 1228; and *Jour. Chem. Soc.*, 1881. p. 829.

finally almost vanishing. $\frac{1}{200}$ of a mgrm. will respond to the test, but it is not in itself conclusive, since papaverine and certain glucosides give an identical reaction.

A test which hitherto has been much relied on, is the blue colour which morphine strikes with neutral chloride of iron. The best way to prepare the solution of iron is to sublime some ferric chloride, and dissolve the product, or (as suggested by Mohr) to use the ferro-ammonium alum.

Symptoms of Opium and Morphine Poisoning.—The symptoms of opium and morphine poisoning are so much alike, that clinically it is impossible to distinguish them; therefore they may be considered together.

Action on Animals—Frogs.—The action of morphine or opium on frogs is peculiar: the animal at first springs restlessly about, and then falls into a condition extremely analogous to that seen in strychnine poisoning, every motion or external irritation producing a tetanic convolution. This condition is, however, sometimes not observed. The tetanic stage is followed by paralysis of reflex movements and cessation of breathing, the heart continuing to beat.

Dogs.—0.2 to 0.5 grm. of morphine meconate, or acetate, injected directly into the circulation of a dog, shows its effects almost immediately. The dog becomes uneasy, and moves its jaws and tongue as if some peculiar taste were experienced; it may bark or utter a whine, and then in a minute or two falls into a profound sleep, which is often so deep that while it lasts—usually several hours—an operation may be performed. In whatever attitude the limbs are placed, they remain. The respiration is rapid and stertorous, and most reflex actions are extinguished. Towards the end of the sleep, any sudden noise may startle the animal, and when he wakes, his faculties are evidently confused. A partial paralysis of the hind legs has often been noticed, and then the dog, with his tail and pelvis low, has something the attitude of the hyena. Hence this condition (first, I believe, noticed by Bernard) has been called the "hyenoid" state. If the dose is larger than 2 to 3 grms. (31 to 46 grains), the symptoms are not dissimilar, save that they terminate in death, which is generally preceded by convulsions.*

*MM. Grasset and Ambard have studied the action of morphine in causing convulsions in the mammalia. They found that if small doses of hydrochlorate of morphine (from 1 to 15 centigrammes) are administered to dogs, the brief sleep which is produced may be accompanied by partial muscular contractions (in one paw, for instance), which are renewed at variable intervals. Then occur true convulsive shocks in the whole body, or in the hind limbs. After an interval the phenomena recur in more intense degree, and are followed by true convulsions. Regularly, ten or sixteen times a minute, at each inspiration, the hind limbs present a series of convulsive movements, which may become general. Sometimes they are excited by external stimulation; but they are usually spontaneous. The sleep may continue profound during this convulsive period, or it may become distinctly lighter. These

Cats show very similar symptoms. Rabbits only sleep, but if the dose is large, convulsions generally are present at the close.

Birds, especially pigeons, are able to eat almost incredible quantities of opium. A pigeon is said * to have consumed 801 grains of opium mixed with its food, in fourteen days. The explanation of this is that the poison is not absorbed; for subcutaneous injections of salts of morphine act rapidly on all birds hitherto experimented upon.

Physiological Action.—From experiments on animals, the essential action of morphine on the nervous and arterial systems has in some measure been examined. There is no very considerable action on the heart. The beats are first accelerated, then diminished in frequency; but very large doses introduced directly into the circulation at once diminish the pulsations, and no acceleration is noticed. The slowing may go on to heart-paralysis. The slowing is central in its origin, for on the vagi being cut, morphine always quickens. With regard to the peripheric ends of the vagi, small doses excite, large paralyse. If all the nerves going to the heart are divided, there is first a considerable acceleration, then a slowing and weakening of the pulsations. The arterial blood-pressure, at first increased, is afterwards diminished. This increase of blood-pressure is noticed during the acceleration of the pulse, and also during some portion of the time during which the pulse is slowed. Gescheidlen, in his researches on the frog, found the motor

convulsive phenomena may continue, with intervals, for an hour. Differences are observed with different animals; but the chief characters of the phenomena are as described. In certain animals, and with small doses, there may be a brief convulsive phase at the commencement of the sleep, but it is much less constant than the later period of spasm. These convulsions, the authors believe, have not previously been described, except as a consequence of very large doses, amounting to grammes. The period of cerebral excitement, described by Claude Bernard as occurring at the commencement of the sleep from morphine is a phenomenon of a different order. The conclusions drawn from the experiments are—(1) That morphia is not diametrically opposed to thebaine as is often stated, since it has, to a certain degree, the convulsive properties of the latter alkaloid. This conclusion is of interest in connection with the researches of Grimaux, just detailed (p. 268). (2) That the excitomotor action of opium cannot be exclusively attributed to the convulsive alkaloids, but is, in fact, due to those which are soporific. According to the ordinary composition of opium, 5 centigrammes of morphine represent about a milligramme of thebaine. But these experiments show that the quantity of morphine has a much more powerful convulsive action than a milligramme of thebaine. (3) There is not the supposed antagonism researches hitherto undertaken on the antagonism between morphine and between the action of morphine on the frog and on the mammalia. (4) The other agents need to be repeated, and a separate study made of the substances which antagonise the convulsive and soporific action.

* Hermann's *Lehrbuch der Exper. Toxicologie*, p. 374.

nerves at first excited, and then depressed. When the doses were large there was scarcely any excitement, but the reverse effect, in the neighbourhood of the place of application. According to other observers, the function of the motor nerves may be annihilated*. According to Meihui-zen reflex action, at first much diminished, is later, after several hours, normal, and later still again, increased. The intestinal movements are transitorily increased. In the dog there has been noticed a greater flow of saliva than usual, and the flow of bile from the gall bladder is diminished. The pupils in animals are mostly contracted, but, if convulsions occur towards death, they are dilated.

Action on Man.—There are at least three forms of opium poisoning:—(1) *The common form*, as seen in about 99 per cent. of cases; (2) a *very sudden form*, in which death takes place with fearful rapidity (the *foudroyante* variety of the French)†; and (3) a very rare entirely *abnormal form*, in which there is no coma, but convulsions.

In the *common form* there are three stages, viz:—(1) excitement; (2) narcosis; (3) coma. In from half an hour to an hour ‡ the first symptoms commence, the pulse is quickened, the pupils are contracted, the face flushes, and the hands and feet reddened,—in other words, the capillary circulation is active. This stage has some analogy to the action of alcohol; the ideas mostly flow with great rapidity, and instead of a feeling of sleepiness, the reverse is the case. It, however, insensibly, and more or less rapidly, passes into the next stage of heaviness and stupor. There is an irresistible tendency to sleep; the pulse and the respiration become slower; the conjunctivæ are reddened; the face and head often flushed. In some cases there is great irritability of the skin, and an eruption of nettle-rash. If the poison has been taken by the mouth, vomiting may be present. The bowels are usually—in fact almost invariably—constipated. There is also some loss of power over the bladder.

In the next stage, the narcosis deepens into dangerous coma; the patient can no longer be roused by noises, shaking, or external stimuli; the breathing is loud and stertorous; the face often pale; the body covered with a clammy sweat. The pupils are still contracted, but they may in the last hours of life dilate; and it is generally agreed that, if a corpse is found with the pupils dilated, this circumstance, taken in itself, does not contra-indicate opium or morphine poisoning. Death occasionally terminates by convulsion.

* *Arch. f. d. Ges. Physiol.*, vii., p. 201.

† Tardieu: *Étude Méd. Légale sur l'Empoisonnement*.

‡ In a remarkable case related by Taylor, a lady took a large dose (supposed to be $1\frac{1}{2}$ oz.) of laudanum, and there were no symptoms for four and a half hours. She died in twenty-two hours.

The *sudden form* is that in which the individual sinks into a deep sleep almost immediately—that is, within five or ten minutes—and dies in a few hours. In these rapid cases the pupils are said to be constantly dilated.

Examples of the *convulsive form* are to be sought among opium-eaters or persons under otherwise abnormal conditions.

A man, forty years old, who had taken opiates daily since his twenty-second year, (his dose being 6 grms. (92·4 grains) of solid opium), when out hunting, of which sport he was passionately fond, took cold, and as a remedy, administered to himself three times his accustomed dose. Very shortly there was a contraction of the left arm, disturbance of vision, pain in the stomach, faintness, inability to speak, and unconsciousness, which lasted half an hour. Intermittent convulsions now set in, and pains in the limbs. There was neither somnolence nor delirium, but great agitation; repeated vomiting and diarrhoea followed. After five hours these symptoms ceased; but he was excessively prostrate.* There was complete recovery.

One may hazard a surmise that, in such a case, tolerance has been established for morphine, but not for other morphine alkaloids in the same degree, and that the marked nervous symptoms were in no small degree the effect of some of the homologous alkaloids, which, in such an enormous dose, would be taken in sufficient quantity to have a physiological action.

There are several instances of a relapsing or remittent form of poisoning—a form in which the patient more or less completely recovers consciousness, and then sinks back into a fatal slumber. One of the best known is the case of the Hon. Mrs. Anson (January, 1859), who swallowed an ounce and a half of laudanum by mistake. After remaining in a comatose condition for more than nine hours, she revived. The face became natural, the pulse steady. She was able to recognise her daughter, and in a thick voice to give an account of the mistake. But this lasted only ten minutes, when she again became comatose, and died in fourteen hours.†

In a Swedish case quoted by Maschka,‡ a girl, nine years old, in weak health and suffering from slight bronchitis, had been given a non-official acetate of morphia lozenge, which was supposed to contain '5 mgrm. (·075 grain) of morphine acetate. She took the lozenge at eight in the

* Demontporcellet: *De l'Usage Quotidien de l'Opium*. Paris, 18·4.

† Taylor, *Op. cit.*

‡ Maschka's *Handbuch*, Band ii., p. 438; also Svenska, *Läk-Scilsk Fördhand*; Apr. 1, p. 90; Apr. 8, p. 160, 173. For other cases see Nasmyth, *Edin. Med. Journ.*, Dec. 1878, Kirby, *Dub. Med. Press*, Dec. 24, 1845; W. Boyd Muschet, *Med. Times and Gaz.*, March 20, 1858.

evening; soon slept, woke at ten, got out of bed, laughed, talked, and joked with the nurse, again got into bed, and very quickly fell asleep. At four a.m. the nurse came and found her breathing with a rattling sound, and the physician, who arrived an hour later, found the girl in a state of coma, with contracted pupils, breathing stertorously, and the pulse scarcely to be felt. Despite all attempts to rouse the patient, she died at eight in the morning, twelve hours after taking the lozenge.

The *post-mortem* examination showed some hyperæmia of the brain and serous effusion in the ventricles, and there was also tubercle in the pleura. Three lozenges similar to the one taken by the patient were chemically investigated by Hamberg, who found that the amount of acetate was very small, and that the lozenges, instead of morphine acetate, might be considered as prepared with almost pure morphine: the content in the three of morphine being respectively 35, 37, and 42 mgrms. (that is, from half a grain to three-fifths of a grain). There was a difference of opinion among the experts as to whether in this case the child died from morphine poisoning or not—a difference solely to be attributed to the waking up of the child two hours after taking the poison. Now, considering the great probability that a large dose for a weakly child of that age had been taken, and that this is not the only case in which a relapse has occurred, it seems just to infer that it was really a case of poisoning.

As unusual symptoms (or rather sequelæ) may be noted in a few cases, hemiplegia, which soon passes off; a weakness of the lower extremities may also be left, and inability to empty the bladder thoroughly; but usually on recovery from a large dose of opium, there is simply heaviness of the head, a dry tongue, constipation, and loss of appetite. All these symptoms in healthy people vanish in a day or two. There have also been noticed slight albuminuria, eruptions on the skin, loss of taste, and numbness of parts of the body.

Opium, whether taken in substance, or still more by subcutaneous injection, in some individuals constantly causes faintness. In my own case, I have several times taken a single grain of opium to relieve either pain or a catarrh; almost invariably within an hour afterwards there has been great coldness of the hands and feet, lividity of the face, a feeling of deadly faintness followed by vomiting; when this stage (which has seldom lasted more than half an hour) had passed, the usual narcotic effects have been produced.

Some years ago I injected one-sixth of a grain of morphine hydrochlorate subcutaneously into an old gentleman, who was suffering from acute lumbago, but was otherwise healthy, and had no heart disease which could be detected; the malady was instantly relieved, and he called out, "I am well; it is most extraordinary." He went out of the

front door, and walked some fifty yards, and then was observed to reel about like a drunken man. He was supported back and laid in the horizontal posture; the face was livid, the pulse could scarcely be felt, and there was complete loss of consciousness. This state lasted about an hour, and without a doubt the man nearly died. Medical men in practice, who have been in the habit of using hypodermic injections of morphine, have had experiences very similar to this and other cases, and although I know of no actual death, yet it is evident that morphine, when injected hypodermically even in a moderate dose, may kill by syncope, and within a few minutes.* Absorption by hypodermic administration is so rapid that by the time, or even before, the needle of the syringe is withdrawn, a contraction of the pupil may be observed.

Opium or morphine is poisonous by whatever channel it gains access to the system; the intestinal mucous membrane absorbs it readily, and narcotic effects may be produced by external applications, whether a wound is present or not. A case of absorption of opium by a wound is related in Chever's "Jurisprudence."[†] A Burman boy, about nine or ten years of age, was struck on the forehead by a brickbat, causing a gaping wound about an inch long; his parents stuffed the wound with opium. On the third day after the accident, and the opium still remaining in the wound, he became semi-comatose, and in short had all the symptoms of opium narcosis; with treatment he recovered. The unbroken skin also readily absorbs the drug. Tardieu states that he had seen 30 grms. of laudanum, applied on a poultice to the abdomen, produce death. Christison has also cited a case in which a soldier suffered from erysipelas, and died in a narcotic state, apparently produced from the too free application of laudanum to the inflamed part.

To these cases may be added the one cited by Taylor, in which a druggist applied 30 grains of morphine to the surface of an ulcerated breast, and the woman died with all the symptoms of narcotic poisoning ten hours after the application—an event scarcely surprising. It is a curious question whether sufficient of the poison enters into the secretions—*e.g.*, the milk—to render it poisonous. An inquest was held in Manchester, Nov., 1875, on the body of a male child two days old, in which it seemed probable that death had occurred through the mother's milk. She was a confirmed opium-eater, taking a solid ounce per week.

Diagnosis of Opium Poisoning.—The diagnosis is at times between poisoning by opium or other narcotic substances, at others, between

* See a case of morphia poisoning by hypodermic injection, and recovery, by Philip E. Hill, M.R.C.S., *Lancet*, Sept. 30, 1882. In this instance a third of a grain introduced subcutaneously caused most dangerous symptoms in a gardener, aged 48.

† 3rd Ed., p. 228.

opium and disease. Insensibility from chloral, from alcohol, from belladonna or atropine, and from carbon oxide gas, are all more or less like opium poisoning. With regard to chloral, it may be that only chemical analysis and surrounding circumstances can clear up the matter. In alcohol poisoning, the breath commonly smells very strongly of alcohol, and there is no difficulty in separating it from the contents of the stomach, &c., besides which the stomach is usually red and inflamed. Atropine and belladonna invariably dilate the pupil, and although just before death opium has the same effect, yet we must hold that mostly opium contracts, and that a widely dilated pupil during life would, *per se*, lead us to suspect that opium had not been used, although, as before mentioned, too much stress must not be laid upon the state of the pupils. In carbon oxide, the peculiar rose-red condition of the body affords a striking contrast to the pallor which, for the most part, accompanies opium poisoning. In the rare cases in which convulsions are a prominent symptom, it may be doubtful whether opium or strychnine has been taken, but the convulsions hitherto noticed in opium poisoning seem to me to have been rather of an epileptiform character, and very different from the effects of strychnine. No rules can be laid down for cases which do not run a normal course; in medicine such are being constantly met with, and require all the care and acumen of the trained observer. Cases of disease render a diagnosis often extremely difficult, and the more so in those instances in which a dose of laudanum or other opiate has been administered. In a case recently under my own observation, a woman, suffering from emphysema and bronchitis, sent to a chemist for a sleeping draught, which she took directly it arrived. A short time afterwards she fell into a profound slumber, and died within six hours. The draught had been contained in an ounce-and-a-half bottle; the bottle was empty, and the druggist stated in evidence that it only contained 20 minims of laudanum, 10 grains of potassic bromide, and water. On, however, diluting the single drop remaining in the bottle, and imitating its colour with several samples of laudanum diluted in the same way, I came to the conclusion that the quantity of laudanum which the bottle originally contained was far in excess of that which had been stated, and that it was over 1 drachm and under 2 drachms. The body was pallid, the pupils strongly contracted, the vessels of the brain membranes were filled with fluid blood, and there was about an ounce of serous fluid in each ventricle. The lungs were excessively emphysematous, and there was much secretion in the bronchi; the liver was slightly cirrhotic. The blood, the liver, and the contents of the stomach were exhaustively analysed with the greatest care, but no trace of morphine, narcotine, or meconic acid could be separated, although the woman did not live more than six hours after taking the draught. I gave the

opinion that it was, in the woman's state, improper to prescribe a sedative of that kind, and that probably death had been accelerated, if not directly caused, by opium.

Deaths by apoplexy will only simulate opium-poisoning during life; a *post-mortem* examination will at once reveal the true nature of the malady. In epilepsy, however, it is different, and more than once an epileptic fit has occurred and been followed by coma—a coma which certainly cannot be distinguished from that produced by a narcotic poison. Death in this stage may follow, and on examining the body no lesion may be found.

Opium-eating.—The consumption of opium is a very ancient practice among Eastern nations, and the picture, drawn by novelist and traveller, of poor, dried-up, yellow mortals addicted to this vice, with their faculties torpid, their skin hanging in wrinkles on their wasted bodies, the conjunctivae tinged with bile, the bowels so inactive that there is scarcely an excretion in the course of a week, the mental faculties verging on idiocy and imbecility, is only true of a percentage of those who are addicted to the habit. Recent researches, and the statements of those who have had the greatest opportunity of observation, show that it is possible for very large doses of opium to be taken by certain people, and yet a high degree of health, both physical and mental, enjoyed. The habitual consumption of opium by individuals has a direct medico-legal bearing. Thus in India, among the Rajpoots, from time immemorial, infused opium has been the drink both of reconciliation and of ordinary greeting, and it is no evidence of death by poison if even a considerable quantity of opium be found in the stomach after death, for this circumstance taken alone would, unless the history of the case was further known, be considered insufficient proof. So, again, in all climates, and among all races, it is entirely unknown what quantity of an opiate should be considered a poisonous dose for an opium-eater. Almost incredible quantities have, indeed, been consumed by such persons, and the commonly-received explanation, that the drug, in these cases, passes out unabsorbed, can scarcely be correct, for Hermann mentions the case of a lady of Zurich who daily injected subcutaneously 1 to 2 grms. (18·4 grains) of a morphine salt. In a case of uterine cancer, recorded by Dr. W. C. Cass,* 20 grains of morphine in the twelve hours were frequently used subcutaneously; during thirteen months the hypodermic syringe was used 1,350 times, the dose each time being 5 grains. It is not credible that an alkaloid introduced into the body hypodermically should not be absorbed.

Opium-smoking is another form in which the drug is used, but it is

* *Lancet*, March 25, 1882. See also Dr. Boulton's case, *Lancet*, March 18, 1882.

an open question as to what poisonous alkaloids are in opium smoke. It is scarcely probable that morphine should be a constituent, for its subliming point is high, and it will rather be deposited in the cooler portion of the pipe. In any case, opium-smoking seems to injure the health of Asiatics but little. Mr. Vice-Consul King, of Kew-Kiang, in a tour through Upper Yangtsoe and Stechnen, was thrown much into the company of junk sailors and others, "almost every adult of whom smoked more or less." He says:—"Their work was of the hardest and rudest, rising at four and working with hardly any intermission till dark, having constantly to strip and plunge into the stream in all seasons, and this often in the most dangerous parts. The quantity of food they ate was simply prodigious, and from this and their work it seems fairly to be inferred that their constitution was robust. The two most addicted to the habit were the pilot and the ship's cook. On the incessant watchfulness and steady nerve of the former the safety of the junk and all on board depended, while the second worked so hard from 3 A.M. to 10 P.M., and often longer, and seemed so independent of sleep or rest, that to catch him seated or idle was sufficient cause for good-humoured banter. This latter had a conserve of opium and sugar which he chewed during the day, as he was able to smoke only at night.

Post-mortem Appearances.—There are no characteristic appearances after death save hyperæmia of the brain and blood-vessels of the membranes, with generally serous effusion into the ventricles. The pupils are sometimes contracted, sometimes dilated, the dilatation occurring, as before mentioned, in the act of dying. The external surface of the body is either livid or pale. The lungs are commonly hyperæmic, the bladder full of urine; still, in not a few cases, there is nothing abnormal, and in no single case could a pathologist, from the appearance of the organs only, declare the cause of death with confidence.

Separation of Morphine from Animal Tissues and Fluids.—Formerly a large proportion of the opium and morphine cases submitted to chemical experts led to no results; but owing to the improved processes now adopted, failure, though still common, is less frequent. The constituents of opium taken into the blood undergo partial destruction in the animal body, but a portion may be found in the secretions, more especially in the urine and faeces. First Bouchardat* and then Lefort† ascertained the excretion of morphine by the urine after medicinal doses; Dragendorff and Hauzmann showed that the appearance of morphine in the urine was constant, and that it could be easily ascertained and separa-

* *Bull. Gén. de Théráp.*, Dec., 1861.

† *Journ. de Chim.*, xi., 93, 1861

ted from the urine of men and animals; and Levinstein* has also shown that the elimination from a single dose may extend over five or six days. The method used by Dragendorff to extract morphine from either urine or blood is to shake the liquid (acidified with a mineral acid) several times with amyl alcohol, which, on removal, separates urea and any bile acids. The liquid thus purified is then alkaliised, and shaken up with amyl alcohol, and this amyl alcohol should contain any morphine that was present. On evaporation it may be pure enough to admit of identification, but if not, it may be redissolved and purified on the usual principles. Considerable variety of results seem to be obtained by different experimenters. Landsberg† injected hypodermically doses of '2 to '4 grm. of morphine hydrochlorate into dogs, making four experiments in all, but failed to detect morphine in the urine. A large dose with 2·4 mgrms. of the salt gave the same result. On the other hand, '8 grm. of morphine hydrochlorate injected direct into the jugular vein, was partly excreted by the kidneys, for 90 cc. of the urine yielded a small quantity of morphine. Voit, again, examined the urine and faeces of a man who had taken morphine for years; he could detect none in the urine, but separated morphine from the faeces.‡ Morphine may occasionally be recognised in the blood. Dragendorff § found it in the blood of a cat twenty-five minutes after a subcutaneous dose, and he also separated it from the blood of a man who died of morphine poisoning in six hours. Haidlen|| recognised morphine in the blood of a suicide who had taken opium extract.

On the other hand, in a case recorded at p. 274, where a woman died in six hours from a moderate dose probably of laudanum, although the quantity of blood operated upon was over a pound in weight, and every care was taken, the results were entirely negative. In poisoning by laudanum there may be some remaining in the stomach, and also, if large doses of morphine have been taken by the mouth; but when morphine has been administered hypodermically, and in all cases in which several hours have elapsed, one may almost say that the organ in which there is the least probability of finding the poison is the stomach. It may, in some cases, be necessary to operate on a very large scale, to examine the faeces, mince up the whole liver, the kidney, spleen, and lungs, and treat them

* *Berl. Klin. Wochenschr.*, 1876, 27.

† *Pflüger's Archiv*, 23, 433, 413-433. *Chem. Soc. Journ.*, May, 1882, 543.

‡ *Arch. Pharm.*, pp. [3.], vii., pp. 23-26.

§ Kauzmann: *Beiträge für den Gerichtlich-Chemischen Nachweis des Morphia u. Narcotins.* Dissert., Dorpat, 1868. Dragendorff: *Pharm. Zeitschr. f. Russland*, 1868, Hft. 4.

|| *Würtzbg. Correspondenzbl.*, xxxiv., 16, 1863.

with acid alcohol. The urine will also have to be examined, and as much blood as can be obtained. In cases where all the evidence points to a minute quantity (under a grain) of morphine, it is decidedly best to add these various extracts together, to distil off the alcohol at a very gentle heat, to dry the residue in a vacuum, to dissolve again in absolute alcohol, filter, evaporate again to dryness, dissolve in water, and then use Dragendorff's process—*i.e.*, extract finally the morphine with amylic alcohol from the solution alkaliised. The expert will, of course, not in such a case, be able to say that he extracted morphine from any particular organ, but rather from the whole body. But does this in a medico-legal case matter?—I think not. Morphine is not a natural constituent of the body; and if it were practicable to mince the whole corpse, treat it with solvents, and, as a result, obtain a small quantity of morphine, such would be a *corpus delicti* of considerable significance. Selmi has pointed out that amylic alcohol extracts from putrefied matters, "ptomaines" agreeing with morphine in setting free iodine from iodic acid; but there has been no ptomaine separated hitherto which gives a precipitate with iodine and hydriodic acid of the definite and identical form of morphine hydriiodide, and which, at the same time, responds to the iodic test. The reaction of Poggiale has been also proposed as an aid in discriminating the ptomaines from morphine. It is possible to detect morphine a long time after death. Stas found the alkaloid thirteen months after burial.

Narcotine ($C_{22}H_{22}NO_7$) crystallises out of alcohol or ether in colourless, transparent, glittering needles, or groups of needles, belonging to the orthorhombic system.

It is only slightly soluble in boiling, and almost insoluble in cold water. One part requires 100 parts of cold, and 20 of boiling 84 per cent. alcohol; 126 parts of cold, 48 of boiling ether (specific gravity 0.735); 2.69 parts of chloroform; 400 of olive oil; 60 of acetic ether; 300 of amyl alcohol; and 22 parts of benzene, for solution. The neutral solution of narcotine turns the plane of polarisation to the left $[a]r = 130.6$; the acid solution to the right.

Narcotine gives no crystalline sublimate; its behaviour in the subliming cell is described at p. 230.

Behaviour of Narcotine with Reagents.—Narcotine, dissolved in dilute hydrochloric acid, and then treated with a little bromine, gives a yellow precipitate, which on boiling is dissolved; by gradually adding solution of bromine and boiling, a fine rose colour is produced, but readily destroyed by excess of bromine. This is perhaps the best test for the presence of narcotine. Concentrated sulphuric acid dissolves narcotine; the solution in the cold is at first colourless, after a few minutes yellow, and in the course of a day or longer the tints gradually deepen. If the solution is warmed, it first becomes orange-red, then at the margin violet-

blue, and if heated until hydric sulphate begins to volatilise, the colour is an intense red-violet. If the heating is not carried so far, but the solution allowed to cool, a delicate cherry-red hue slowly develops. If the sulphuric acid solution contains 1:2000 of the alkaloid, this test is very evident; with 1:40,000, the colour is only a faint carmine (A. Husemann.)

A solution of narcotine in pure sulphuric acid, to which a drop of nitric acid has been added, becomes of a red colour; if the solution is warmed to 150°, hypochlorite of soda develops a carmine-red; and chloride of iron first a violet, then a cherry-red. The precipitants of narcotine are—phosphomolybdic acid, picric acid, sulphocyanide of potash, potassium cadmic iodide, mercuric chloride, platinic chloride, auric chloride, and several other reagents.

From the brown mass left after heating narcotine above 200°, hydrochloric acid extracts a small portion of a base but little studied. The residue consists of humopic acid ($C_{40}H_{19}N_{14}$), which can be obtained by dissolving in caustic potash, precipitating with HCl, dissolving the precipitate in boiling alcohol, and finally throwing it down by water.

Effects.—Narcotine in itself has toxic action only in rather large doses; from 1 to 2 grms. have been given to man, and slight hypnotic effects have followed. It is poisonous in very large doses; an ordinary sized cat is killed by 3 grms. The symptoms are mainly convulsions.

Codeine ($C_{18}H_{21}NO_3$) is an alkaloid contained in opium in small quantity only. Mulder, indeed, quotes 66 to 75 per cent. as present in Smyrna opium, but Merck and Schindler give 25 per cent. Schindler found, in Constantinople, 5 per cent.; and Merck, in Bengal, 5 per cent. also. Codeine is considered by Grimaux to be an ether of morphine; he has proposed for it the name of *codomethylene*.

Codeine crystallises out of dry ether in small, colourless, anhydrous crystals; but crystallised slowly from an aqueous solution, the crystals are either in well-defined octahedra, or in prisms, containing one atom of water, and melting in boiling water to an oily fluid.

It requires 80 parts of cold, 17 of boiling water, 10 parts of benzole, and 7 parts of amyl alcohol respectively, for solution. Alcohol, benzene, ether, and chloroform freely dissolve it, but in petroleum ether it is almost insoluble. Further, it is also soluble in aqueous ammonia, and in dilute acids, but insoluble in excess of caustic potash or soda, and may thus be thrown out of an aqueous solution. A solution of codeine turns the plane of polarisation to the left, $[a]r = 118.2^\circ$.

Concentrated sulphuric acid dissolves codeine without colour, but after eight days the solution becomes blue; this reaction is quicker if the acid contains a trace of nitric acid. If the sulphuric acid solution be warmed to 150°, and a drop of nitric acid be added after cooling, a blood

red colour is produced. Fröhde's reagent produces a dirty green colour, soon becoming Prussian blue, and terminating after twenty-four hours in a pale yellow.

Cyanogen gas, led into an alcoholic solution of codeine, gives first a yellow and then a brown colour; lastly, a crystalline precipitate falls. On warming with a little sulphuric acid and ferric chloride, a blue colour is produced. This blue colour is apparently common to all ethers of the codeine class.

Effects.—The physiological action of codeine on animals has been investigated by Claude Bernard, Magendie, Crum Brown and Fraser, Falck, and a large number of others.* It has also been administered to man, and has taken in some degree the place of morphine. Claude Bernard showed that, when given to dogs in sufficient quantity to produce sleep, the sleep was different in some respects to that of morphine sleep, especially in its after-effects. Thus, in his usual graphic way, he describes the following experiment:—"Two young dogs, accustomed to play together, and both a little beyond the average size, received in the cellular tissue of the axillæ, by the aid of a subcutaneous syringe, the one 5 centigrammes of morphine hydrochloride, the other 5 centigrammes of codeine hydrochloride. At the end of a quarter of an hour both dogs showed signs of narcosis. They were placed on their backs in the experimental trough, and slept tranquilly for three or four hours. When the animals woke, they presented the most striking contrast. The morphine dog ran with a hyena-like gait (*démarche hyénoid*), the eye wild, recognising no one, not even his codeine comrade, who vainly bit him playfully, and jumped sportively on his back. It was not until the next day that the morphine dog regained his spirits and usual humour. A couple of days after, the two dogs being in good health, I repeated the same experiment, but in an inverse order—that is to say, I gave the codeine to that which previously had the morphine, and *vice versa*. Both dogs slept about as long as the first time; but on waking the attitudes were completely reversed, just as the administration of the two substances had been. The dog which, two days before, after having been codeinised, woke lively and gay, was now bewildered and half paralysed at the end of his morphine sleep; whilst the other was wide awake and in the best spirits.

Subsequent experimenters found what Bernard does not mention—viz., that codeine produced epileptiform convulsions. Falck made some very careful experiments on pigeons, frogs, and rabbits. To all these in high enough doses it was fatal. Falck puts the minimum lethal dose for a rabbit at 51.2 mgrms. per kilo. Given to man, it produces a sleep very

* *Ann. Chem. Phys.* [5], 27, pp. 273-288; also, *Jour. Chem. Soc.*, No. ccxliv., 1883, p. 358.

similar to that described by Claude Bernard—that is, a sleep which is very natural, and does not leave any after-effect. Therefore, it is declared to be the best alkaloid of a narcotic nature to give when lengthened slumber is desired, more especially since it does not confine the bowels, nor has it been found to produce any eruption on the skin. Before it has a full narcotic effect, vomiting has often been excited, and in a few cases purging. The maximum dose for an adult is about 1 grm. (1.5 grains); three times this quantity, 3 grms. (4.5 grains), would probably produce unpleasant, if not dangerous, symptoms.*

Narceine ($C_{23}H_{29}NO_9$) crystallises out of water, alcohol, or diluted acetic acid, in long, white, four-sided, rhombic prisms, or fine, bushy, united needles. It has a somewhat bitter taste, and is without odour.

The crystals generally contain water of crystallisation. One part of narceine dissolves in 375 parts of cold, 230 of boiling water. Very concentrated potash-lye precipitates narceine from its watery solution as an oil, weaker alkaline liquids dissolve it. One part of narceine is dissolved in 945 parts of 80 per cent. alcohol. It is easily soluble in boiling alcohol and in hot acetic acid, but is insoluble in ether. Benzole and petroleum ether extract narceine neither from acid nor alkaline solutions; chloroform extracts narceine both from acid and from alkaline solutions, the latter in small proportion only. Narceine turns the plane of polarisation to the left, $a[r] = 66.7^\circ$. Narceine may be separated from narcotine by the addition of ammonia to the acid aqueous solution; narcotine is fully precipitated by ammonia, but narceine is left in solution.

It melts at 134° , but gives no crystalline sublimate. The melted substance is at first colourless; but on raising the temperature, the usual transitions of colour through different shades of brown to black are observed. If melted, and kept a few degrees above its melting point, and then cooled slowly, the residue is straw-coloured, divided into lobes, most of which contain feathery crystals.

At high temperatures narceine develops a herring-like odour; the residue becomes darkish blue with iron chloride. Concentrated nitric acid dissolves it with a yellow colour; on heating, red vapours are produced; the fluid contains crystals of oxalic acid, and develops with potash a volatile base. Concentrated sulphuric acid colours pure narceine brown; but if impure, a blood-red or blue colour may be produced.

Fröhde's reagent colours it first brown-green, then red, passing into blue. Narceine forms precipitates with bichromate of potash, chloride of gold, bichloride of platinum, and several other reagents. The one

* For further details as to the action of codeine, the reader is referred to L. O. Wach's monograph, *Das Codein* (1868), which contains reference to the earlier literature. See also Harley, "The Old Vegetable Neurotics." London.

formed by the addition of potassio zinc iodide is in hair-like crystals, which after twenty-four hours become blue.

Weak iodine solution colours narceine crystals a black-blue; they dissolve in water at 100° without colour, but on cooling again separate with a violet or blue colour. A drop of "Nessler" solution, added to solid narceine, at once strikes a brown colour; on diluting the drop with a little water, beautiful little bundles of crystals appear.

Effects.—The physiological action of narceine has been variously interpreted by different observers. Claude Bernard* thought it the most somniferous of the opium alkaloids. He said that "the narceinic sleep was characterised by a profound calm and absence of the excitability of morphine, the animals narcotised by narceine on awaking returning to their natural state without enfeeblement of the hind limbs or other sequelæ." It has been amply confirmed that narceine possesses somniferous properties, but certainly not to the extent that Bernard's observations led physiologists to expect. In large doses there is some irritation of the stomach and intestines, and vomiting occurs, and even diarrhoea; moderate doses induce constipation. The maximum medicinal dose may be put at 1·4 grm. (or 2·26 grains), and a probable dangerous dose would be three times that quantity.†

Papaverine ($C_{21}H_{31}NO_4$) crystallises from alcohol in white needles or scales. It possesses scarcely any alkaline reaction, and has but little effect on a ray of polarised light. It is almost insoluble in water; alcohol and ether dissolve it in the cold with difficulty; boiling, copiously, but the alkaloid partly separates on cooling. One part of the alkaloid is dissolved in 36·6 of benzene, and in 76 parts of amyl alcohol. Petroleum ether dissolves it by the aid of heat, but the alkaloid separates in crystals on cooling. Chloroform extracts it from either acid or alkaline solutions. Papaverine gives no crystalline sublimate. It melts at 130°; the residue is amorphous, light brown, and is not characteristic. Concentrated sulphuric acid colours it a deep violet-blue, and dissolves it to a violet, slowly fading. This solution, by permanganate of potash, is first green and then gray. Fröhde's reagent gives a beautiful violet colour, which becomes blue, and vanishes after twenty-four hours. Diluted solutions of salts of papaverine are not precipitated by phosphomolybdic acid. It is precipitated by ammonia, by the caustic and carbonated alkalies, by potassic-cadmic iodide, iodine in hydriodic acid, and by alkaloidal reagents generally—save by the important exception mentioned above. A

* *Comp. Rend.*, lix. p. 406, 1864.

† See J. Bouchardat, *La Narcéine, Thèse*, Paris, 1865; Harley, "The Old Vegetable Neurotics," Lond.; Ch. Liné. *Etudes sur la Narcéine et son Emploi Thérapeutique, Thèse*, Paris, 1865; also Husemann's *Planzenstoffe*, in which these and other researches are summarised.

olution in amyl alcohol is also precipitated by bromine ; the precipitate is crystalline. An alcoholic solution of platinic chloride also separates papaverine platin chloride in crystals. An alcoholic solution of iodine, added to an alcoholic solution of papaverine, separates in a little time crystals of the composition of $C_{21}H_{21}NO_4I_2$. From the mother-liquor, by concentration, can be obtained needles of another iodine combination, $C_{21}H_{21}NO_4I_3$; the latter heated above 100° parts with free iodine. These compounds with iodine are decomposed by ammonia and potash, papaverine separating. The decomposition may be watched under the microscope. Papaverine may be assumed to be present if a substance is separated, which gives (1) a violet colour with Fröhde's reagent ; (2) a dense white precipitate with cadmio-potassic iodide ; (3) no precipitate with phosphomolybdic acid ; and (4) a precipitate of needles, if to an alcoholic solution of the alkaloid an alcoholic solution of iodine is added.

Effects.—Claude Bernard ranked papaverine with the convulsants ; probably the papaverine he had was impure. In any case, subsequent observations have shown that it is to be classed rather with the hypnotic principles of opium. Leidesdorf* administered it to the insane, and noted slowness of the pulse, muscular weakness, and drowsiness to follow. The doses were given subcutaneously (42 grm. of the hydrochloride). Baxt,† experimenting with the frog, found that a milligramme caused deep sleep and slowing of the heart's action. This action on the heart is witnessed also on the recently-removed frog's heart. Guinea pigs and other small animals poisoned by strychnine or thebaine, and then given papaverine, did not seem to be so soon affected with tetanus as when no such remedy was administered. The fatal dose of papaverine for a man is unknown. I should conjecture that the least quantity that would cause dangerous symptoms would be 1 grm. (15·4 grains).

Thebaine ($C_{19}H_{21}NO_3$).—Opium seldom contains much more than 1 per cent. of this alkaloid. It usually forms needles or short crystals. It is strongly alkaline, and by rubbing becomes negatively electric. It is almost insoluble in water, aqueous ammonia, and solutions of the alkalies. It requires 10 parts of cold alcohol for solution, and dissolves readily in hot. Ether, hot or cold, is also a good solvent. 100 parts of benzene are required for 5·27 parts of thebaine, and 100 of amyl alcohol for 1·67 parts. Chloroform dissolves thebaine with difficulty out of both acid and alkaline solutions ; petroleum ether extracts it from neither. Thebaine sublimes at 135° . The sublimate is in minute crystals, similar to theine : at higher temperatures (160° to 200°) needles, cubes, and prisms are obtained. The residue is fawn coloured. Fröhde's

* *Ztschr. d. Wien. Aerzte*, pp. 18, 115, 1868.

† *Arch. Anat., Phys.*, p. 70, 1869.

reagent (as well as concentrated sulphuric acid) dissolves it, with the production of a blood-red colour, passing gradually into yellow. The precipitate with picric acid is yellow and amorphous; with tannic acid, yellow; with gold chloride, red-yellow; and with platinic chloride, citron-yellow, gradually becoming crystalline. A concentrated alcoholic solution of thebaine, just neutralised with HCl, deposits well-formed rhombic crystals of the composition $C_{19}H_{21}NO_3HCl + H_2O$.

Effects.—There is no disagreement of opinion as to the action of thebaine. By the united testimony of all who have experimented with it, the alkaloid belongs to those poisons which produce tetanus, and the symptoms can scarcely be differentiated from strychnia. In Baxt's experiments on frogs he showed that there was some considerable difference in details in the general course of the symptoms, according to the dose of the poison. A small dose (such, for example, as '75 mgrm.) injected into a frog subcutaneously produces immediate excitement, the animal jumping about, and this stage lasting for about a minute; it then becomes quieter, and has from three to six minutes' sleep; in a little time this comatose state is followed by reflex tetanic spasms and then spontaneous tetanic spasms. With three times the dose, the tetanic convulsions commence early, and death takes place in from two to six hours. Baxt* found 6 to 7 mgrms. kill rabbits with tetanic convulsions in from fifteen to twenty-five minutes. Crum Brown and Fraser also found that 12 mgrms. injected into rabbits were fatal; it may then be presumed that the lethal dose for a rabbit is about 5 mgrms. per kilo. A frog's heart under the action of thebaine, and removed from the body, beats quicker and ceases earlier than one in distilled water. Thebaine has been administered to the insane subcutaneously in doses of from 12 to 40 mgrms., when a rise of temperature and an increase in the respiratory movements and in the circulation were noticed.†

The fatal dose for a man is not known; '5 grms., or about 8 grains, would probably be a poisonous quantity.

Cryptopine ($C_{23}H_{28}NO_6$) was discovered by T. & H. Smith in 1867.‡ It is only contained in very minute traces in opium—something like '003 per cent. It is a crystalline substance, the crystals being colourless, six-sided prisms, without odour, but with a bitter taste, causing an after-sensation like peppermint. The crystals melt at $203\cdot3^\circ$, and congeal in a crystalline form again at 171° ; at high temperatures they are decomposed with evolution of ammoniacal vapour. Cryptopine is insoluble, or almost so, in ether, water, oil of turpentine, and benzene; chloroform is the best solvent, or hot alcohol; it is insoluble in aqueous ammonia.

* *Sitzungsber. d. Wien. Akadem.*, lvi., pp. 2, 89, 1867. *Arch. f. Anat. u. Physiol.*, Hft. 1, p. 112, 1869.

† F. W. Müller, *Das Thebaine. eine Monographie*. Diss., Marburg, 1868.

‡ *Pharm. Jour. Trans.* (2), viii., pp. 495 and 716.

in solutions of the caustic alkaloids. Cryptopine is strongly basic, neutralising mineral acids. Concentrated sulphuric acid colours cryptopine pure the tint gradually fading from absorption of water from the atmosphere. crystal of potassic nitrate being added, the colour changes into a permanent a. With ferric chloride cryptopine gives no colour—thus distinguishing it morphine. The physiological properties of cryptopine have been investigated by Dr. Harley,* it has a narcotic action, about double as strong as narceine, four times weaker than morphine. Munk and Sippell † found that it gave in animals to paralytic paralysis of the limbs, and occasionally asphyxic unctions before death.

Rhaeadine ($C_{21}H_{21}NO_6$)—Rhœadine was separated from *Papaver rh* as by e, and has also been found in *Papaver somniferum* and in opium. Rhœadine the form of small anhydrous tasteless prisms, melting at 230° and partly ming. In a vacuum sublimation is almost complete, and at a much lower erature. It is a very insoluble substance, and is scarcely dissolved, when talline, by water, alcohol, ether, chloroform, benzene, and solutions of the l or volatile alkalies. When in an amorphous state it is rather soluble in r, and may be dissolved out of any substance by treating with dilute acetic and neutralising by ammonia, and shaking up with ether before the pre ate becomes crystalline. Rhœadine is easily recognized by the intense blue colour produced by dissolving a little of the substance in dilute sulphuric or ochloric acid. Either spontaneously or on gentle warming, the colour is prod—one part of rhœadine will colour in this way 10,000 parts of acid-water or purple-red, 200,000 rose-red, and 800,000 pale-red. The reaction depends splitting up of the rheadine into a colourless substance, *rhaedin*, and a red iring matter. Rhœadine is not poisonous.

Pseudomorphine ($C_{17}H_{19}NO_4$).—Pseudomorphine was discovered by Pelletier Thiboumery in 1835. As precipitated by ammonia out of the hot solution, domorphine falls as a white crystalline precipitate; but if the solution is cold, precipitate is gelatinous. It possesses no taste, and has no action on vegetal colours. On heating, it decomposes, and then melts. It dissolves easily in tic alkalies and in milk of lime, but is insoluble in all the ordinary alcoholic ethereal solvents, as well as in diluted sulphuric acid. The most soluble salt e hydrochlorate ($C_{17}H_{19}NO_4HCl + H_2O$), and that requires 70 parts of water at for solution. Various salts, such as the sulphate, oxalate, &c., may be pre d from the hydrochlorate by double decomposition. Concentrated sulphuric dissolves pseudomorphine gradually, with the production of an olive-green ir.

Opianine ($C_{68}H_{72}N_4O_{21}$).—Opianine crystallises in colourless, glittering, orthobic needles. Ammonia precipitates it from its solution in hydrochloric acid fine white powder. It is without odour, and has a bitter taste. It is a strong , and is soluble in cold, but slightly soluble in boiling water. It is also butly soluble in boiling alcohol.

An alcoholic solution of the alkaloid gives a voluminous precipitate with curic chloride; after standing a little time, the precipitate becomes crystal the crystals being in the shape of fine needles. They have the following

* "The Old Vegetable Neurotics."

† Munk, *Versuche über die Wirkung des Cryptopins*. Berlin, 1873. Sippell age zur Kentniss des Cryptopins. Marburg, 1874.

composition— $C_{66}H_{72}N_4O_{21}, 2HCl, 2HgCl$ —and are with difficulty soluble in water or alcohol.

Opianine administered to cats in doses of 145 grm., produces complex symptoms—e. g., dilated pupils, foaming at the mouth, uncertain gait, paralysis of the hinder extremities, and stupor,—but the alkaloid is rare, and few experiments have been made with it.

Apomorphine ($C_{17}H_{19}NO_3$).—Apomorphine is a derivative of morphine, and is readily prepared by saponifying morphine by heating it with dilute hydrochloric acid in sealed tubes. The result is apomorphine hydrochloride, the morphine losing one molecule of water, according to the equation $C_{17}H_{19}NO_3 = C_{17}H_{18}NO_2 + H_2O$.

To extract apomorphine, the bases are precipitated by sodic bicarbonate, and the precipitate extracted by ether or chloroform, either of which solvents leaves morphine undissolved. The apomorphine is again converted into hydrochloride, and once more precipitated by sodic bicarbonate, and is lastly obtained as a snow-white substance rapidly becoming green on exposure to the air. The mass dissolves with a beautiful green colour in water, and also in alcohol, whilst it colours ether purple-red, and chloroform violet.

Apomorphine is the purest and most active emetic known ; whether injected beneath the skin or taken by the mouth, the effect is the same—there is considerable depression, faintness, and then vomiting. The dose for an adult is about 6 mgrms. (.092 grain) subcutaneously administered.

The reactions of some of the rarer alkaloids of opium with sulphuric acid and ferric chloride are as follows : none of them have at present any toxicological importance :—

TABLE XI.—SOME REACTIONS OF THE RARER ALKALOIDS OF OPIUM.

Alkaloid.	Formula.	Reaction with Warm Sulphuric Acid.	Reaction with Ferric Chloride.
Codamine,	$C_{20}H_{26}NO_4$	Dirty red violet colour, turning dark violet on the additional HNO_3 .	Dark green.
Landamine,	$C_{20}H_{26}NO_4$		
Landanosine,	$C_{21}H_{27}NO_4$	Dirty green to brownish green.	No colour.
Protapine,	$C_{20}H_{29}NO_5$		
Lanthopine,	$C_{23}H_{26}NO_4$	Dark brown or black.	No colour.
Hydrocotarnine,	$C_{12}H_{16}NO_2$	Dirty red-violet; not changed by trace of HNO_3 .	No colour.

Meconin (Opianyl) ($C_{10}H_{16}O_4$) is in the form of white glittering needles, which melt under water at 77° and in air at 90° , again coagulating at 75° . It may be sublimed in beautiful crystals. It is soluble in 22 parts of boiling, and 700 of cold,

r ; dissolves easily in alcohol, ether, acetic acid, and ethereal oil, and is not precipitated by the acetate of lead. Its solution in concentrated sulphuric acid turns, on warming, purple, and gives, on the addition of water, a brown precipitate. Meconin may be prepared by treating narcotine with nitric acid. Meconin, in large doses, is a feeble narcotic, and 1·25 grm. (20 grains) has been given an without result.

Meconic Acid ($C_7H_4O_7$) crystallises in white shining scales or small rhombic prisms, with three atoms of water ($C_7H_4O_7 + 3H_2O$), but at 100° this is lost, and it becomes an opaque white mass. It reddens litmus, and has a sourish taste. It is soluble in 115 parts of cold, but dissolves in four parts of boiling, water ; it dissolves easily in alcohol, less so in ether. It forms well-marked salts ; the barium and calcium salt crystallise with one atom of water, the former having the composition $BaH_4(C_7H_4O_7)$; the latter, if ammonium meconate is precipitated by calcium chloride, $C_6H_4(C_7H_4O_7)_2$; but if calcium chloride is added to the acid itself, it also has the composition $C_7H_4C_6O_7 + H_2O$. If meconic acid is gently heated, it decomposes into carbon dioxide and meconic acid ($C_6H_4O_5$). If the heat is greater, pyromeconic acid ($C_6H_4O_5$)—carbon dioxide, water, acetic acid, and benzene are formed. Pyromeconic acid is readily sublimed in large transparent scales. Chloride of iron, and soluble iron salts generally give with meconic acid (with great dilution) a lively red colour, which is not altered by heat, nor by addition of HCl, nor by that of gold chloride. Sugar of lead and nitrate of silver each give a white precipitate ; and mercurous and mercuric nitrates white yellow precipitates. In any case where the analyst has found only meconic acid the question may be raised in court as to whether it is a poison or not. The experiments of Serturner,* Langer, Vogel, Sömmerring, and Gräfe† showed in comparatively speaking large doses it had but little, if any, action on animals or men. Albers‡ has, however, experimented on frogs, and found that in doses of 1 to 2 grm. there is, first, a narcotic action, and later, convulsions and death. According to Schroff,§ there is a slight narcotic action on man.

The most generally accepted view at the present time is that the physiological action of meconic acid is similar to that of lactic acid—viz., small doses cause some depression and feeble narcosis.

In a special research amongst organic fluids for meconic acid, the substances are extracted by alcohol *feebly* acidulated with nitric acid ; on evaporation the alcohol, after the addition of a little water, is distilled off, and to the remaining fluid a solution of acetate of lead is added, and the solution is filtered. The filtrate will contain any alkaloids, whilst meconic acid, if present, is bound up with the lead on the filter. The meconate of lead may be either washed or digested in strong acetic acid, to purify it, and it is then suspended in water, and freed from lead by SH_2 ; the filtrate from the sulphide may be tested by ferric chloride, or preferably, at once

* *Ann. Phys.*, xxv. 56 ; xxvij., 187.

† *De opio et de illis quibus constat partibus*. Berol., 1822.

‡ *Arch. Path. Anat.*, xxvij., 248.

§ *Med. Jahresh.*, 1869.

evaporated to dryness, and weighed. After this operation it is identified. If the quantity is so small that it cannot be conveniently weighed, it may be estimated colorimetrically, by having a standard solution of meconic acid, containing 1 mgrm. in every cc. A few drops of neutral ferric chloride are added in a Nessler cylinder to the liquid under examination; and the tint thus obtained is imitated in the usual way, in another cylinder, by means of ferric chloride, the standard solution and water. It is also obvious that the weight of the meconic acid may be increased by converting it into the barium salt—100 parts of anhydrous baric meconate, BaH_4 (C_7HO_7)₂, being equivalent to 74.5 of meconic acid ($\text{C}_7\text{H}_4\text{O}_7$).

IV.—THE STRYCHNINE OR TETANUS-PRODUCING GROUP OF ALKALOIDS.

1. NUX VOMICA GROUP—STRYCHNINE—BRUCINE—IGASURINE.

Nux vomica is found in commerce both in the entire state and as a powder. It is the seed of the *Strychnos nux vomica*, or Koochla tree. The seed is about the size of a shilling, round, flattened, concavo-convex, of a yellowish-grey or light-brown colour, covered with a velvety down of fine, radiating, silky hairs, which are coloured by a solution of iodine beautiful gold-yellow; the texture is tough, leathery, and not easily pulverised; the taste is intensely bitter. The powder is not unlike that of liquorice, and, if met with in the pure state, gives a dark orange-red colour with nitric acid, which is destroyed by chloride of tin; the aqueous infusion gives a precipitate with tincture of galls, is reddened by nitric acid, and gives an olive-green tint with persulphate of iron. The best method, however, of recognising quickly and with certainty that the substance under examination is *nux vomica* powder, is to extract strychnine from it by the following simple process:—The powder is completely exhausted by boiling alcohol (90 per cent),* the alcoholic extract evaporated to dryness, and then treated with water; the aqueous solution is passed through a wet filter, and concentrated by evaporation to a small bulk. To this liquid a drop or so of a concentrated solution of chromate of potash is added, and the yellow precipitate of chromate of strychnine thus obtained is separated, and identified both by its forms and by the colour reactions to be described.

* To this group also belong some of the opium alkaloids.—See "Thebaine," "Landamine," "Codeine," "Hydrocotarnine."

Chemical Composition.—*Nux vomica* contains at least four distinct principles—

- (1.) Strychnine.
- (2.) Brucine.
- (3.) Igasurine.
- (4.) Strychnic or igasuric acid.

Strychnine ($C_{21}H_{22}N_2O_2$) is contained in the bean of *S. ignatius*, in the bark (*false angustura bark*) and seeds of the *Strychnos nux vomica*, in the *Strychnos colubrina*, L., in the *Strychnos tienté*, Lesch, and probably in various other plants of the same genus.

Commercial strychnine is met with either in colourless crystals or as a white powder, the most usual form being that of the alkaloid itself; but the nitrate, sulphate, and acetate are also sold to a small extent.

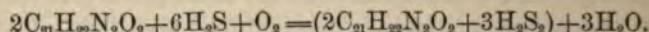
The *microscopical appearance* of strychnine, as thrown down by the solution or vapour of ammonia, may be referred to three leading forms—the long rectangular prism, the short hexagonal prism, or the regular octahedron. If obtained from the slow evaporation of an alcoholic solution, it is usually in the form of four-sided pyramids or long prisms; but if obtained by speedy evaporation or rapid cooling, it appears as a white granular powder. If obtained from a benzene solution, the deposit is usually crystalline, but without a constant form, though at times the crystals are extremely distinct, the short six-sided prism prevailing; but triangular plates, dodecahedral, rhomboidal, and pentagonal, may also be met with. An ethereal solution on evaporation assumes dendritic forms, but may contain octahedra and four-sided prisms. A chloroform solution deposits rosettes, veined leaves, stellate dotted needles, circles with broken radii, and branched and reticulated forms of great delicacy and beauty (*Guy*).

Strychnine is very insoluble in water, although readily dissolved by acidulated water. According to Wormley's repeated experiments, one part of strychnine dissolves in 8,333 parts of cold water: and, according to Pelletier and Cahor, it dissolves in 6,667 parts of cold, and 2,500 parts of boiling, water. It may be convenient, then, to remember that a gallon of cold water would hardly dissolve more than 10 grains (·142 grm. per litre); the same amount, if boiling, about 30 grains (·426 grm. per litre). The solubility of one part of strychnine in other menstrua is as follows:—Cold alcohol, 0·833 specific gravity, 120, boiling, 10 parts (*Wittstein*); cold alcohol, 0·936 specific gravity, 240 parts (*Merck*); cold alcohol, 0·815 specific gravity, 107 parts (*Dragendorff*); amyl alcohol, 181 parts; benzene, 164; chloroform, 6·9 (*Schlümpf*), 5 (*Pettenkofer*). Creasote and essential and fixed oils also dissolve strychnine.

Of all the above solvents, it is evident that chloroform is the best for purposes of separation, and next to chloroform, benzene.

If a speck of strychnine be placed in the subliming cell, it will be found to sublime usually in a crystalline form at 169° . A common form at this temperature, according to the writer's own observations, is minute needle's disposed in lines; but, as Dr. Guy has remarked, the sublimate may consist of drops, of waving patterns, and various other forms; and, further, while the sublates of morphia are made up of curved lines, those of strychnine consist of lines either straight or slightly curved, with parallel feathery lines at right angles. On continuing the heat, strychnine melts at about 221° , and the lower disc, if removed and examined, is found to have a resinous residue; but it still continues to yield sublates until reduced to a spot of carbon.

Strychnine is so powerfully bitter, that one part dissolved in 70,000 of water is distinctly perceptible; it is a strong base, with a marked alkaline reaction, neutralising the strongest acids fully, and precipitating many metallic oxides from their combinations, often with the formation of double salts. Most of the salts of strychnine are crystalline, and all extremely bitter. Strychnine, in the presence of oxygen, combines with SH_2 to form a beautiful crystalline compound:—



On treatment with an acid this compound yields H_2S_2 (Schmidt: *Ber. Deutsch. Chem. Ges.*, 8, 1267).

An alcohol solution of strychnine turns the plane of polarisation to the left, $[a] r = -132.08^{\circ}$ to 136.78° (*Bouchardat*); but acid solutions show a much smaller rotatory power.

The salts used in medicine are—the *sulphate*, officinal only in the French pharmacopœia; the *nitrate*, officinal in the German, Austrian, Swiss, Norse, and Dutch pharmacopœias; and the *acetate*, well known in commerce, but not officinal.

The commercial *Sulphate* ($\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2\text{H}_2\text{SO}_4 + 2\text{H}_2\text{O}$) is an acid salt crystallising in needles which lose water at 150° , the neutral sulphate ($2\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2\text{H}_2\text{SO}_4 + 7\text{H}_2\text{O}$) crystallises in four-sided, orthorhombic prisms, and is soluble in about 50 parts of cold water.

The *Nitrate* ($\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2\text{HNO}_3$) crystallises on evaporation from a warm solution of the alkaloid in dilute nitric acid, in silky needles, mostly collected in groups. The solubility of this salt is considerable, one part dissolving in 50 of cold, in 2 of boiling, water; its solubility in boiling and cold alcohol is almost the same, taking 60 of the former and 2 of the latter.

The *Acetate* crystallises in tufts of needles ; as stated, it is not officinal in any of the European pharmacopœias.

The chief precipitates or sparingly-soluble crystalline compounds of strychnine are—

(1.) The *Chromate of Strychnine* ($C_{21}H_{22}N_2O_2CrHO_3$), formed by adding a neutral solution of chromate of potash to a solution of strychnine salt, crystallises out of hot water in beautiful, very insoluble, orange-yellow needles, mixed with plates of various size and thickness. The salt is of great practical use to the analyst ; for by its aid strychnine may be separated from a variety of substances, including brucine—the colour tests being either applied direct to the strychnine chromate, or the chromate decomposed by ammonia, and the strychnine recovered from the alkaline liquid by chloroform.

(2.) *Sulphocyanide of Strychnine* ($C_{21}H_{22}N_2O_2CNHS$) is a thick, white precipitate, produced by the addition of a solution of potassic sulphocyanide to that of a strychnine salt ; on warming it dissolves, but on cooling reappears in the form of long silky needles.

(3.) *Double Salts*.—The platinum compound obtained by adding a solution of platinic chloride to one of strychnine chloride has the composition $C_{21}H_{22}N_2O_2HClPtCl_2$, and crystallises out of weak boiling alcohol (in which it is somewhat soluble) in gold-like scales. The similar palladium compound ($C_{21}H_{22}N_2O_2HCl$, $PdCl$) is in dark brown needles, and the gold compound ($C_{21}H_{22}N_2O_2HClAuCl_3$) in orange-coloured needles.

(4.) *Strychnine Trichloride*.—The action of chlorine on strychnine—by which chlorine is substituted for a portion of the hydrogen—has been proposed as a test. The alkaloid is dissolved in very dilute HCl, so as to be only just acid ; on now passing through chlorine gas, a white insoluble precipitate is formed, which may be recrystallised from ether ; it has probably the composition $C_{21}H_{19}Cl_3N_2O_2$, and is extremely insoluble in water.

(5.) *The Iodide of Strychnine* ($C_{21}H_{22}N_2O_2HI_3$) is obtained by the action of iodine solution on strychnine sulphate ; on solution of the precipitate in alcohol, and evaporation, it forms violet-coloured crystals, very similar to those of potassic permanganate.

Pharmaceutical and other Preparations of Nux Vomica and Strychnine, with Suggestions for their Valuation.

An aqueous extract of *nux vomica*, officinal in the German pharmacopœia, appears to contain principally brucine, with a small percentage of strychnine ; the proportion of brucine to strychnine being about four-fifths to one-fifth. Blossfield found in a sample 4·3 per cent. of total alkaloid, and two samples examined by Grundmann consisted (No. 1) of strychnine, 0·6 per cent., brucine, 2·58 per cent. ; total, 3·18 per cent. ; (No. 2) strychnine, 0·68 per cent., brucine, 2·62 per cent.—total, 3·3 per

cent. A sample examined by Dragendorff yielded, strychnine, 0·8 per cent., brucine, 3·2 per cent.—total, 4 per cent. The maximum medicinal dose is put at '6 grms. ($9\frac{1}{4}$ grains).

The spirituous extract of nux vomica, officinal in the British and all the Continental pharmacopœias, differs from the aqueous in containing a much larger proportion of alkaloids, the total percentage varying from 7 to 8·6 per cent., and about half the total quantity being strychnine. The maximum medicinal dose is put at '15 grm. (2·3 grains).

There is also an *extract of St. Ignatius bean*, which is used in the United States, and is more active than the extract of *nux vomica*, since nearly the whole of its alkaloid may be referred to strychnine.

The tincture of nux vomica varies somewhat in strength. Liebh found in one sample 0·122 per cent. of strychnine and 0·09 per cent. brucine; and two samples examined by Wissel consisted respectively of 0·353 per cent., and 0·346 per cent., of total alkaloids. Dragendorff found in two samples '2624 per cent. and '244 per cent. of total alkaloids, about half of which was strychnine.

Analysis.—Either of the extracts may be treated for a few hours on the water-bath, with water acidulated by sulphuric acid, filtered, the residue well washed, the acid liquid shaken up with benzene to separate impurities, and, on removal of the benzene, alkalised with ammonia, and shaken up two or three times with chloroform; the chloroform is then evaporated in a tared vessel, and the total alkaloids weighed. Strychnine, as before stated, may be separated from brucine by dissolving the latter out with absolute alcohol. The tincture is analysed on precisely similar principles, the spirit being got rid of by distillation, and the residue treated by acidified water, &c.

The *nux vomica* powder itself may be valued as follows:—15 to 20 grms., pulverised as finely as possible, are treated three times with 150 to 300 cc. of water, acidified with sulphuric acid, well boiled, and, after each boiling, filtered and thoroughly pressed. The last exhaustion must be destitute of all bitter taste. The united filtrates are then evaporated to the consistence of a thick syrup, which is treated with sufficient burnt magnesia to neutralise the acid. The extract is now thoroughly exhausted with boiling alcohol of 90 per cent.; the alcoholic extract, in its turn, is evaporated nearly to dryness, and treated with acidulated water; this acid solution is freed from impurities by shaking up with benzene, and lastly alkalised with ammonia, and the alkaloids extracted by shaking up with successive portions of chloroform. The chloroformic extract equals the total alkaloids, which may be separated in the usual way.

In four samples of *nux vomica* examined by Dragendorff, the total alkaloids ranged from 2·33 to 2·42 per cent. Grate found in two samples 2·88 per cent. and 2·86 per cent. respectively; while Karing from

one sample separated 1.65 per cent. The strychnine and brucine are in about equal proportions, Dragendorff* finding 1.187 per cent. strychnine and 1.145 per cent. brucine.†

The *vermin-killers* in use in this country are—Miller's rat powder, Battle's vermin-killer, and Butler's vermin-killer.

Miller's rat-powder consists of 1 oz. of *nux vomica* and 1 lb of oatmeal—*i.e.*, about 5.3 per cent. of *nux vomica*. Since the average amount in *nux vomica*, strychnine, and brucine is 1.28 per cent. of each, the probability is that this powder contains .068 per cent. of strychnine and the same quantity of brucine.

Battle's vermin-killer (according to an analysis by Tardieu) contains the following in each packet :—

Strychnine,	0.10
Potato Starch,	1.00
Prussian Blue,	0.20
<hr/>	
	1.30 grms.

In other words, each packet weighs 19 grains (or nearly a scruple) and contains 1½ grains of strychnine, or about 7.7 per cent.

Butler's vermin-killer is a mixture of flour, soot, and strychnine, but sometimes Prussian blue is substituted for soot. It is sold in threepenny and sixpenny packets. The latter Taylor found to weigh a drachm (3.8 grms.), and to contain from 2 to 3 grains (.13 to .19 grms.) of strychnine ; the threepenny packet about half this quantity.

The amount of strychnine and brucine in Miller's rat-powder is valued exactly as in the case of *nux vomica* powder.

Battle's or Butler's vermin-powder merely requires exhaustion by benzene or chloroform ; if not pure, purification is easy on well-known principles.

Statistics.—In England, during the five years 1875-80, out of 1,581 total deaths from poison, strychnine and *nux vomica* account for 79. To these deaths an uncertain number, returned under the term “vermin-

* Dragendorff, *Die Chemische Werthbestimmung einiger Starkwirkenden Drogen*. St. Petersburg, 1874.

† These details are very necessary, as bearing on the question of the fatal dose of *nux vomica*, which Taylor tells us (*Med. Jurisprud.*, i. 409) was of some importance in *Reg. v. Wren*, in which 47 grains were attempted to be given in milk. The fatal dose of *nux vomica* must be ruled by its alkaloidal content, which may be so low as 1 per cent., and as high as nearly 3 per cent. 30 grains have proved fatal (*Taylor*) ; if the powder in this instance was of the ordinary strength, the person died from less than a grain (.0648 grm.) of the united alkaloids.

killer," must be added ; from this cause were registered 122. "Vermin-killer" may be presumed to include not only strychnine mixtures, but also phosphorous and arsenic pastes and powders, so that there are no means of ascertaining the number of strychnine cases comprised under this heading. Taking the deaths actually registered as due to strychnine or *nux vomica*, they are about 5 per cent. of the deaths from all sorts of poison. Of these 79 deaths, 67, or less than 83·5 per cent., were suicidal, 3 were homicidal, and 10 only were accidental. The sexes were nearly equally divided, 40 being males, and 39 females ; with regard to age, 4 were under fifteen years of age, 39 between fifteen and thirty-five, the remainder from above thirty-five up to sixty-five.

Schauenstein has collected from literature 130 cases of poisoning by strychnine, but most of these occurred during the last twenty-five years ; 62 of the 130, or about one-half, were fatal, and 15 were homicidal. It has been stated that strychnine is so very unsuitable for the purpose of criminal poisoning as to render it unlikely to be often used. Facts, however, do not bear out this view ; for allowing its intensely bitter taste, yet it must be remembered that bitter liquids, such as bitter ale, are in daily use, and a person accustomed to drink any liquid rapidly might readily imbibe sufficient of a toxic liquid to produce death before he was warned by its bitterness. It is, indeed, capable of demonstration, that taste is more vivid *after* a substance has been taken than just in the act of swallowing, for the function of taste is not a rapid process, and requires a very appreciable interval of time.

Fatal Dose.—In a research, which may for its painstaking accuracy be called classical, F. A. Falck has thrown much light upon the minimum lethal dose of strychnine for various animals. It would seem that, in relation to its size, the frog is by no means so sensible to strychnine as was believed, and that animals such as cats and rabbits take a smaller dose in proportion to their body-weight. The method used by Falck was to inject subcutaneously a solution of known strength of strychnine nitrate, and, beginning at first with a known lethal dose, a second experiment was then made with a smaller dose, and if that proved fatal, with a still smaller, and so on, until such a quantity was arrived at, that the chances as determined by direct observation were as great of recovery as of death. Operating in this way, and making no less than 20 experiments on the rabbit, he found that the least fatal dose for that animal was ·6 mgrm. of strychnine nitrate per kilogramme. Cats were a little less susceptible, taking ·75 mgrm. Operating on fowls, he found that strychnine taken into the crop in the usual way was very uncertain ; 50 mgrms. per kilo. taken with the food had no effect, but results always followed if the poison was introduced into the circulation by the subcutaneous needle.

—the lethal dose for fowls being under these circumstances 1 to 2 mgrms. per kilo. He made 35 experiments on frogs, and found that to kill a frog by strychnine nitrate, at least 2 mgrms. per kilo. must be injected. Mice take a little more, from 2.3 to 2.4 mgrms. per kilo. In two experiments on the ring adder, in one 62.5 mgrms. per kilo. of strychnine nitrate, injected subcutaneously, caused death in seven hours; in the second, 23.1 mgrms. per kilo. caused death in five days; hence the last quantity is probably about the least fatal dose for this particular snake.

These observations may be conveniently thrown into the following Table (see next page), placing the animals in order according to their relative sensitiveness.*

Now, the important question arises, as to the place in this series occupied by man—a question difficult to solve, because so few cases are recorded in which strychnine has been administered by subcutaneous injection with fatal result. Eulenberg has observed poisonous symptoms, but not death, produced by 6 mgrms. ($\frac{1}{11}$ grain) and by 10 mgrms. (about one-sixth grain). Bois observed poisonous symptoms from the similar subcutaneous administration of 8 mgrms. to a child six years old, and 4 mgrms. to another child four years old—the latter dose, in a case recorded by Christison, actually killing a child of three years of age. On the other hand, the smallest lethal dose taken by an adult was swallowed in solution. Dr. Warner took 32 mgrms. ($\frac{1}{2}$ grain) of strychnine sulphate, mistaking it for morphine sulphate, and died in twenty minutes. In other cases 48 mgrms. ($\frac{7}{10}$ grain) have been fatal. It will be safe to conclude that these doses by the stomach would have acted still more surely and energetically if injected subcutaneously. The case of Warner is exceptional, for he was in weak health; and if calculated out according to body-weight, presuming that Dr. Warner weighed 68 kilos., the relative dose as strychnine nitrate would be .24 per kilo.—a smaller dose than for any animal hitherto experimented upon. There is, however, far more reason for believing that the degree of sensitiveness in man is about the same as that of cats or dogs, and that the least fatal dose for man is .70 per kilo., the facts on record fairly bearing out this view. It is, therefore, probable that death would follow if 48 mgrms. ($\frac{7}{10}$ grain) were injected subcutaneously into a man of the average weight of 68 kilos. (150 lbs.) Taylor estimates the fatal dose of strychnine for

* According to Christison's researches, .02 grm. (about $\frac{1}{3}$ grain) is fatal to swine; .03 grm. ($\frac{1}{2}$ grain) to bears, if injected into the pleura. 1 to 3 grains (.0648 to .1944 grm.) is given to horses in cases of paralysis, although 3 grains cannot but be considered a dangerous dose, unless smaller doses have been previously administered without effect; 10 grains would probably kill a horse, and 15 grains (.972 grm.) have certainly done so.

TABLE XII.—ACTION OF STRYCHNINE ON ANIMALS.

Animal	Manner of Application	Reckoned on 1 Kilo. of Body-weight.	
		Lowest Experimental Lethal Dose.	Highest Experimental Lethal Dose.
		Dose of Strychnine Nitrate in Mgrms.	
Rabbit, . . .	Subcutaneous.	0.59	0.80
Cat,	"	..	0.75
Dog,	"	..	0.75
"	Taken by the Stomach.	2.0	8.90
"	2.00
"		5.50	..
Fox,	Subcutaneous.	..	1.00
Hedgehog, . .	"	1.00	2.00
Fowl,	"	..	2.00
Frog,	"	2.00	2.10
Mouse,	"	2.86	2.86
Ring Adder, . .	"	..	23.10

adults as from 32.4 to 129.6 mgrms. (.5 to 2 grains); Guy puts the minimum at 16.2 mgrms. (.25 grains.)

Large doses of strychnine may be recovered from if correct medical treatment is sufficiently prompt. Witness the remarkable instances on record of duplex poisonings, in which the would-be suicide has unwittingly defeated his object by taking strychnine simultaneously with some narcotic, such as opium or chloral. In a case related by Schauenstein* a suicidal pharmacist took .48 grm. or .6 grm. (7.4 to 9.25 grains of strychnine nitrate dissolved in about 30 cc. of bitter almond water, and then, after half an hour, since no symptoms were experienced, .6 grm. (9.25 grains) of morphine acetate, which he likewise dissolved in bitter-almond water and swallowed. After about ten minutes, he still could walk with uncertain steps, and poured some chloroform on the pillow-case of his bed, and lay on his face in order to breathe it. In a short

* Maschka's *Handbuch*, from Tschepke: *Deutsche Klinik*, 1861.

time he lost consciousness, but again awoke, and lay in a half-dreamy state, incapable of motion, until some one entered the room, and hearing him murmur, came to his bedside. At that moment—two and a quarter hours after first taking the strychnine—the pharmacist had a fearful convulsion, the breathing was suspended, and he lost consciousness. Again coming to himself, he had several convulsions, and a physician who was summoned found him in general tetanus. There were first clonic, then tonic convulsions, and finally opisthotonus was fully developed. The treatment consisted of emetics, and afterwards tannin and codein were given separately. The patient slept at short intervals ; in ten hours after the taking of the poison the seizures were fewer in number and weaker in character, and by the third day recovery was complete. Dr. Macredy* has also placed on record an interesting case, in which the symptoms, from a not very large dose of strychnine, were delayed by laudanum for eight hours. A young woman, twenty-three years of age, pregnant, took at 10 A.M. a quantity of strychnine estimated at 1·5 grain, in the form of Battle's vermin-killer, and immediately afterwards 2 ounces of laudanum. She was seen by Dr. Macredy in four hours, and was then suffering from pronounced narcotic symptoms. A sulphate of zinc emetic was administered. In eight hours after taking the strychnine, there were first observed some clonic convulsive movements of the hands, and, in a less degree, the legs. These convulsions continued, at times severe, for several hours, and were treated with chloral. Recovery was speedy and complete.

In a similar case related by Dr. Harrison,† a man, aged 54, took a packet of Battle's vermin-killer, mixed with about a drachm and a half of laudanum and some rum. At the time he had eaten no food for days, and had been drinking freely ; yet fifty minutes elapsed before the usual symptoms set in, and no medical treatment was obtained until four hours after taking the dose. He was then given chloral and other remedies, and made a rapid recovery.

Action on Animals.—The action of strychnine has been experimentally studied on all classes of animals, from the infusoria upwards. The effects produced on animal forms which possess a nervous system are strikingly alike, and even in the cephalopodo, tetanic muscular spasm may be readily observed. Of all animals the frog shows the action of strychnine in its purest form, especially if a dose be given of just sufficient magnitude to produce toxic effects. The frog sits perfectly still and quiet, unless acted upon by some external stimuli, such as a breath of air, a loud noise, or the shaking of the vessel which contains it, then

* *Lancet*, November, 28 1882.

† *Lancet*, May 13, 1882.

an immediate tetanic convulsion of all the muscles is witnessed, lasting a few seconds only, when the animal again resumes its former posture. This heightened state of reflex action has its analogue in hydrophobia as well as in idiopathic tetanus. If the frog thus poisoned by a weak dose is put under a glass shade, kept moist, and sheltered from sound or from other sources of irritation, no convulsions occur, and after some days it is in its usual health. If, on the other hand, by frequent stimuli, convulsions are excited, the animal dies. M. Richet* has lately contributed a valuable memoir to the Academy of Sciences on the toxic action of strychnine. He has confirmed the statement of previous observers that, with artificial respiration, much larger doses of strychnine may be taken without fatal result than under normal conditions, and has also recorded some peculiar phenomena. Operating on dogs and rabbits, after first securing a canula in the trachea, and then injecting beneath the skin or into the saphena vein 10 mgrms. of strychnine hydrochlorate, the animal is immediately, or within a few seconds, seized with tetanic convulsions, and this attack would be mortal, were it not for artificial respiration. Directly this is practised the attack ceases, and the heart, after a period of hurried and spasmoidic beats, takes again its regular rhythm. Stronger and stronger doses may then be injected without causing death. As the dose is thus augmented, the symptoms differ. M. Richet distinguishes the following periods:—(1) A period of tetanus. (2) A period of convulsion, characterised by spasmoidic and incessant contraction of all the muscles. (3) A little later, when the quantity exceeds 10 mgrms. per kilo., a choreic period, which is characterised by violent rhythmic shocks, very sudden and short, repeated at intervals of about three to four seconds; during these intervals there is almost complete relaxation. (4) A period of relaxation; this period is attained when the dose exceeds 40 mgrms. per kilo. Reflex action is annihilated, the spontaneous respiratory movements cease, the heart beats tumultuously and regularly in the severe tetanic convulsions at first, and then contracts with frequency but with regularity. The pupils, widely dilated at first, become much contracted. The arterial pressure, enormously raised at the commencement, diminishes gradually, in one case from 0.34 mm. to 0.05 mm. The temperature undergoes analogous changes, and during the convulsions is extraordinarily elevated; it may even attain 41° or 42°, to sink in the period of relaxation to 36°. Dogs and rabbits which have thus received enormous quantities of strychnine (*e. g.*, 50 mgrms. per kilo.) may, in this way, live for several hours, but the slightest interrup-

* *De l'Action de la Strychnine à très forte dose sur les Mammifères. Comptes Rend., t. xcl., p. 181.*

tion to the artificial respiration, in the relaxed state, is followed by syncope and death.

Effects on Man: Symptoms.—The commencement of symptoms may be extremely rapid, the rapidity being mainly dependent on the form of the poison and the manner of application. A soluble salt of strychnine injected subcutaneously will act within a few seconds*; in a case of amaurosis, related by Schuler,† 5.4 mgrms. of a soluble strychnine salt were introduced into the *Punctum lachrymate*;—in less than four minutes there were violent tetanic convulsions. In a case related by Barker, the symptoms commenced in three minutes from a dose of .37 grm. (5.71 grains). Here the poison was not administered subcutaneously. Such short periods, to a witness whose mind was occupied during the time, might seem immediate. On the other hand, when *nux vomica* powder has been taken, and when strychnine has been given in the form of pill, no such rapid course has been observed, or is likely to occur, the usual course being for the symptoms to commence within half an hour. It is, however, also possible for them to be delayed from one to two hours, and under certain circumstances (as in the case related by Macredy) for eight hours. In a few cases, there is first a feeling of uneasiness and heightened sensibility to external stimuli, a strange feeling in the muscles of the jaw, and a catching of the respiration; but generally the onset of the symptoms is as sudden as epilepsy, and previous to their appearance the person may be pursuing his ordinary vocation, when, without preliminary warning, there is a shuddering of the whole frame, and a convulsive seizure. The convulsions take the form of violent general tetanus; the limbs are stretched out involuntarily, the hands are clenched, the soles of the feet incurved, and, in the height of the paroxysm, the back may be arched and rigid as a board, the sufferer resting on head and heels, and the abdomen tense. In the grasp of the thoracic muscles the walls of the chest are set immovable, and from the impending suffocation the face becomes congested, the eyes prominent and staring. The muscles of the lower jaw—in “disease tetanus” the first to be affected—are in “strychnos tetanus,” as a rule, the last; a distinction, if it were more constant, of great clinical value. The convulsions and remissions recur until death or recovery, and, as a rule, within two hours from the commencement of the symptoms the case in some way or other terminates. The number of the tetanic seizures noted has varied—in a few cases the third spasm has passed into death, in others there have been a great number. The duration of the spasm is also very different, and

* In one of M. Richet's experiments, a soluble strychnine salt injected into a dog subcutaneously acted in fourteen seconds.

† Quoted by Taylor from *Med. Times and Gazette*, July, 1861.

varies from thirty seconds to five or even eight minutes, the interval between lasting from forty-five seconds* to one or even one and a half hours.†

Diagnosis of Strychnine Poisoning.—However striking and well defined the picture of strychnine tetanus may be, mistakes in diagnosis are rather frequent, especially when a medical man is hastily summoned, has never seen a case of similar poisoning, and has no suspicion of the possible nature of the seizure. If a young woman, for instance, is the subject, he may put it down to hysteria, and certainly hysteria not unfrequently affects somewhat similar convulsions. In a painful case in which the author was engaged, a young woman either took or was given (for the mystery was never cleared up fully) a fatal dose of strychnine, and though the symptoms were well marked, the medical attendant was so possessed with the view that the case was due to hysteria, that, even after making the *post-mortem* examination, and finding no adequate lesion he theorised as to the possibility of some fatal hysterical spasm of the glottis, while there was ample chemical evidence of strychnine, and a weighable quantity of the alkaloid was actually separated from the contents of the stomach. Such cases are particularly sad, for we now know that, with judicious treatment, a rather large dose may be recovered from.

If the case is a male, a confusion with epilepsy is possible, though hardly to be explained or excused; while in both sexes idiopathic tetanus is so extremely similar as to give rise to the idea that all cases of idiopathic tetanus are produced by poison, perhaps secreted by the body itself. As for the distinction between idiopathic and strychnic tetanus, it is usually laid down (1) that the intervals in the former are characterised by no relaxation of the muscles, but that they continue contracted and hard; and (2) that there is a notable rise of temperature in disease tetanus proper, and not in strychnine tetanus. Both statements are misleading, and the latter is not true, for in strychnic poisoning the relaxation is not constant and very high temperatures in animals have been observed.

Physiological Action.—The tetanic convulsions are essentially reflex, and to be ascribed to a central origin; the normal reflex sensibility is exaggerated and unnaturally extended. If the ischiatic plexus supplying the one leg of an animal is cut through, that leg takes no part in the general convulsions, but if the artery of the leg alone is tied, then the leg suffers from the muscular spasm, as well as the limbs in which the circulation is unrestrained. In an experiment by Dr. W. B. Richardson, a healthy dog was killed, and, as soon as practicable, a

* White, *Brit. Med. Journ.*, 1867.

† Folkes, *Med. Times*, 1869.

solution of strychnine was ejected through the systemic vessels by the aorta—the whole body became at once stiff and rigid as a board. These facts point unmistakably to the spinal marrow as the seat of the toxic influence. Strychnine is, *par excellence*, a spinal poison. On physiological grounds, the gray substance of the cord is considered to have an inhibitory action upon reflex sensibility, and this inhibitory power is paralysed by strychnine.

Much light has been thrown upon the cause of death by Richet's experiments.* It would seem that, in some cases, death takes place by a suffocation as complete as in drowning, the chest and diaphragm being immovable, and the nervous respiratory centres exhausted. In such a case, immediate death would be averted by a tracheal tube, by the aid of which artificial respiration might be carried on; but there is another asphyxia due to the enormous interstitial combustion carried on by muscles violently tetanised. "If," says Richet, "after having injected into a dog a mortal dose of strychnine, and employed artificial respiration according to the classic method twenty or thirty times a minute, the animal dies (sometimes at the end of ten minutes and in every case at the end of an hour or two), and during life the arterial blood is examined, it will be ascertained that it is black, absolutely like venous blood."

This view is also supported by the considerable rise of temperature noticed: the blood is excessively poor in oxygen, and loaded with carbon dioxide. That this state of the blood is produced by tetanus, is proved by the fact that an animal poisoned by strychnine, and then injected subcutaneously with curare in quantity just sufficient to paralyse the muscular system, does not exhibit this phenomena. By the aid of artificial respiration, together with the administration of curare, an animal may live after a prodigious dose of strychnine.

Meyer † has investigated carefully the action of strychnine on the blood-pressure—through a strong excitement of the vaso-motor centre, the arteries are narrowed in calibre, and the blood-pressure much increased; the action of the heart in frogs is slowed, but in the warm-blooded quickened.

Post-mortem Appearances.—There is but little characteristic in the *post-mortem* appearances from strychnine poisoning. The body becomes very stiff a short time after death, and this rigidity remains generally a long time. In the notorious Palmer case, the body was rigid two months after death, but, on the other hand, the *rigor mortis* has been known to disappear within twenty-four hours. If the convulsions have been vio-

* *Op. cit.*

† *Wiener Akad. Sitzungsber.*, 1871.

lent, there may be minute haemorrhages in the brain and other parts. I have seen considerable haemorrhage in the trachea from this cause. When death occurs from asphyxia, the ordinary signs of asphyxia will be found in the lungs, &c. The heart mostly has its right side gorged with blood, but in a few cases it is empty and contracted.

In a case which Schauenstein has recorded * he found strychnine still undissolved, coating the stomach as a white powder; but this is very unusual, and I believe unique. The bladder often contains urine, which, it need scarcely be said, should be preserved for chemical investigation.

Treatment.—From the cases detailed, and from the experiments on animals, the direction which treatment should take is very clear. As a matter of course, if there is the slightest probability of any of the poison remaining in the stomach, it should be removed either by emetics, or, better, by the stomach-pump. Large and frequent doses of chloral should be administered in order to lessen the frequency of convulsions, or prevent their occurrence, and it may be necessary in a few cases, where death threatens by suffocation, to perform tracheotomy, and to use artificial respiration. Where chloral or chloroform is not at hand, and in cases of emergency, where this may easily happen, the medical man must administer in full doses the nearest narcotic at hand.†

Separation of Strychnine from Organic Matters.—The separation of strychnine from organic matters, &c., is undertaken strictly on the general principles already detailed. It may happen, however, that in cases of poisoning there is the strongest evidence from symptoms in the person or animal that strychnine alone is to be sought for. In an instance of the kind, if a complex organic liquid (such as the contents of the stomach) is under examination, it is best to remove the solid substances by filtration through glass, wool, or linen, and evaporate nearly to dryness over the water-bath, acidifying with acetic acid, and then exhausting the residue repeatedly with boiling alcohol of 80 per cent. The alcohol extract is in its turn evaporated to dryness, and taken up with water; the aqueous solution is passed through a wet filter, and then shaken up with the usual succession of fluids—viz., petroleum ether, benzene, chloroform, and amyl alcohol, which will remove a great number of impurities, but will not dissolve the strychnine from the acid solution. The amyl alcohol may lastly be removed by petroleum ether; and on removal of

* *Op. cit.*

† It is certain that lutidine would be a valuable antidote for strychnine. C. G. Williams found that lutidine injected into frogs already under the influence of strychnine, arrested the convulsions, or if given first, and then followed by a fatal dose of strychnine, it prevented the appearance of the tetanus. (See *ante*, p. 247, foot note.)

the final extractive (which should be done as thoroughly as possible) chloroform is added, and the fluid is alkaliised by ammonia, which precipitates the alkaloid in presence of the solvent. Should the reverse process be employed—that is, ammonia added first, and then chloroform—the strychnine is not so perfectly dissolved, since it has time to assume a crystalline condition. On separation and evaporation of the chloroform, the residue (if much discoloured, and evidently impure) may be dissolved in alcohol or benzene, and recrystallised several times; this by practice can be done without any loss of substance.

Should search be made for minute portions of strychnine in the tissues, considering the small amount of poison which may produce death, it is absolutely necessary to operate on a very large quantity of material. It would be advisable to take the whole of the liver, the brain, spinal cord, spleen, stomach, duodenum, kidneys, and all the blood that can be obtained, and a considerable quantity of muscular tissue, so as to make in all about one-eighth to one-tenth of the whole body; this may be cut up into small pieces, and boiled in capacious flasks with alcohol, acidified with acetic acid. Evaporation must be controlled by adapting to the cork an upright condenser.

Should the analyst not have apparatus of a size to undertake this at one operation, it may be done in separate portions—the filtrate from any single operation being collected in a flask, and the spirit distilled off in order to be used for the next. In this way, a large quantity of the organs and tissues can be exhausted by half a gallon of alcohol. Finally, most of the alcohol is distilled off, and the remainder evaporated at a gentle heat in a capacious dish, the extract being treated by water, &c., as described. It is only by working on this large scale that there is any probability of detecting absorbed strychnine in those cases where only one or two grains have destroyed life, and even then it is possible to miss the poison.

Strychnine may be separated from the urine by concentrating to about one-third of its bulk, acidifying with sulphuric acid, and filtering; a mixture of equal volumes of ether and chloroform is added, and the urine then alkaliised by ammonia and shaken. The ether chloroform subsides to the bottom, and may be drawn off, and on evaporation leaves the strychnine present, mixed, of course, with some impurities. A more thorough extraction of strychnine from urine is to evaporate to syrup, alkaliise by caustic potash, treat the alkaline syrup with repeated quantities of chloroform, separate the chloroform, and drive it off by the gentle heat of a water-bath. The residue is now digested for some time with concentrated sulphuric acid on the water-bath, again made alkaline, and extracted by chloroform. This final chloroform extract will leave the

alkaloid in a fairly pure state, and it may be converted into chromate, and the sulphuric acid test applied.

Strychnine is separated by the kidneys rapidly. In a suicidal case recorded by Schauenstein,* death took place in an hour and a half after taking strychnine, yet from 200 cc. of the urine, Schauenstein was able to separate nitrate, of strychnine in well-formed crystals. Dr. Kratter* has made some special researches on the times within which strychnine is excreted by the kidneys. In two patients, who were being treated by subcutaneous injection, half an hour after the injection of 7.5 mgrms. of strychnine nitrate, the alkaloid was recognised in the urine. The strychnine treatment was continued for eight to ten days, and then stopped; two days after the cessation, strychnine was found in the urine, but none on the third day, and the inference drawn is that the elimination is complete within forty-eight hours.

Strychnine has been detected in the blood of dogs and cats in researches specially undertaken for that purpose, but sometimes a negative result has been obtained, without apparent cause. Dragendorff † gave dogs the largest possible dose of strychnine daily. On the first few days no strychnine was found in the urine, but later it was detected, especially if food was withheld. M'Adam was the first who detected the absorbed poison, recognising it in the muscles and urine of a poisoned horse, and also in the urine of a hound. Dragendorff has found it in traces in the kidneys, spleen, and pancreas; Gay, in different parts of the central nervous system, and in the saliva. So far as the evidence goes, the liver is the best organ to examine for strychnine; but all parts supplied with blood, and most secretions, may contain small quantities of the alkaloid. At one time it was believed that strychnine might be destroyed by putrefaction, but the question of the decomposition of the poison in putrid bodies may be said to be settled. So far as all evidence goes, strychnine is an extremely stable substance, and no amount of putrescence will destroy it. M'Adam found it in a horse a month after death, and in a duck eight weeks after; Nunneley in fifteen animals forty-three days after death, when the bodies were much decomposed; Roger in a body after five weeks interment; and lastly, Richter in putrid tissues exposed for eleven years to decomposition in open vessels.

Identification of the Alkaloid.—A residue containing strychnine, or strychnine mixed with brucine, is identified—

(1.) By its alkaline reaction and its bitter taste. No substance can possibly be strychnine unless it taste markedly bitter.

* Maschka's *Handbuch*, Band 2, p. 620.

† In an animal rapidly killed by a subcutaneous injection of acetate of strychnine, no strychnine was detected either in the blood or liver.—*Dragendorff*.

(2.) By the extremely insoluble chromate of strychnine, already described.* A fluid containing 1 : 1000 of strychnine gives with chromate of potash (if allowed to stand over night) a marked precipitate, dissimilar to all others, except those of lead and baryta chromates, neither of which can possibly occur if any of the processes described are followed.

(3.) If the chromate just described is treated on a porcelain plate with a drop of pure strong sulphuric acid, a deep rich blue colour, passing through purple into red, rapidly makes its appearance. Dr. Guy, neglecting intermediate colours, aptly compares the succession—(1) to the rich blue of the Orleans plum ; (2) to the darker purple of the mulberry ; and (3) to the bright clear red of the sweet orange. These characters—viz., alkalinity, bitterness, and the property of precipitation by potassic chromate in a definite crystalline form, the crystals giving the colours detailed—belong to no other substance known save strychnine, and for all purposes sufficiently identify the alkaloid. Other tests are as follows :—

(4.) Colours similar to (3) may also be obtained by mixing a drop of sulphuric acid with strychnine and a crystal, or speck of any one of the following substances :—Ferridecyanide of potash, permanganate of potash, peroxide of lead, or peroxide of manganese.

(5.) Its behaviour in the subliming cell has been already described ; tests may be applied to any of the sublimates, or to the substance itself. Dr. Guy has proposed to treat a sublimate with a drop of solution of dilute picric acid, $\frac{1}{250}$. In a few seconds or minutes, small, round, greenish-brown spots show themselves, which spread, often coalesce, and become the centres of delicate arborescent crystalline groups, the elementary form in all of which is a large section of a small circle, a rare form, and one eminently characteristic.

(6.) Letheby's galvanic colour test :—If a minute strychnine residue, obtained by the evaporation of a drop of dilute solution of strychnine in a cup-shaped depression in a piece of platinum foil, be treated with a drop of concentrated sulphuric acid, and the foil connected with the positive pole of a Grove or Smee's battery, on touching the acid with the negative pole a violet colour flashes out, and on removing the pole the tint remains.

(7.) Sonnenschein has proposed the sesquioxide of cerium and sulphuric acid as a test for strychnine : the colours produced are a beautiful blue, passing slowly into violet, and terminating in a long-enduring cherry-red.

The colour tests are supposed to be employed upon the more or less pure substance. If, however, strychnine be mixed with no great quan-

* 1 grm. of strychnine gave 1.280 grms. of the chromate, —78.1 per cent. of strychnine ; 3 gave 3.811 of the chromate, —78.77 per cent. of strychnine.—*Mohr.*

ty of starch or dextrine, tarter emetic, tartaric acid, or argol, it will still respond.

Brucine, if in large quantity, renders the tests for strychnine uncertain ; but, as already pointed out, the strychnine may be converted into chromate, and thus separated from brucine. The pharmaceutical preparations, moreover, do not contain sufficient brucine to interfere seriously with colour tests. In mixture with santonin it is easily detected. Dragendorff obtained evidence of its presence when only so small a quantity as '32 mgrm. was present. In mixture with quinine and cinchonine it can also be detected. Dragendorff was able to render evident '025 mgrm. mixed with twenty times its weight of quin. sulphate ; the same observer likewise recognised '04 mgrm. of strychnine in thirty-three times its weight of caffeine. Veratrine is likewise not injurious. Since morphine is used as an antidote, it might be separated with strychnine ; Reese* recognised in a mixture of equal parts of strychnine and morphine, $\frac{1}{50000}$ grm. when the proportion was 1:2 ; $\frac{1}{30000}$ grm. when 1:3 ; $\frac{1}{15000}$ grm. when 1:4 ; $\frac{1}{10000}$ grm. when 1:5 ; $\frac{1}{8000}$ grm. when 1:10 ; $\frac{1}{1000}$ grm. when 1:20 ; but these alkaloids are easily separated, absolute alcohol dissolving out the morphine, and leaving the strychnine.

(8.) *The Physiological Test* consists in administering the substance to some small animal (preferably to a frog), and inducing the ordinary tetanic symptoms. It may be at once observed that if definite chemical evidence of strychnine has been obtained, the physiological test is quite unnecessary ; and, on the other hand, should the application of a liquid or substance to a frog induce tetanus, while chemical evidence of the presence of strychnine was wanting, it would be hazardous to assert that strychnine was present, seeing that caffeine, carbolic acid, picrotoxin, certain of the opium alkaloids, some of the ptomaines, and many other substances induce similar symptoms. The best method (if the test is used at all) is to take two frogs,† and insert under the skin of the one the needle of the subcutaneous syringe, previously charged with a solution of the substance, injecting a moderate quantity. The other frog is treated similarly with a very dilute solution of strychnine, and the two are then placed under small glass shades, and the symptoms observed and compared. It is not absolutely necessary to inject the solution under the skin, for if applied to the surface the same effects are produced ; but, if accustomed to manipulation, the operator will find the subcutaneous ap-

* *Pharm. Zeitschr. f. Russland. Jahrg.*, i., p. 277.

† A very practical disadvantage of the physiological test is the great difficulty of obtaining frogs exactly when wanted.

plication more certain, especially in dealing with minute quantities of the alkaloid.*

Brucine ($C_{23}H_{28}N_2O_4$)† occurs associated with strychnine in the plants already mentioned ; its best source is the so-called *false angustura* bark, which contains but little strychnine. Its action is similar to that of strychnine. If crystallised out of dilute alcohol it contains 4 atoms of water, easily expelled either in a vacuum over sulphuric acid or by heat. Crystallised thus, it forms transparent four-sided prisms, or arborescent forms, like boric acid. If thrown down by ammonia from a solution of the acetate, it presents itself in needles or in tufts.

The recently-crystallised alkaloid has a solubility different from that which has effloresced, the former dissolving in 320 parts of cold, and 150 parts of boiling water ; whilst the latter (according to Pelletier and Caventou) requires 500 of boiling, and 850 parts of cold, water for solution. Brucine is easily soluble in absolute, as well as in ordinary, alcohol ; 1 part dissolves in 1.7 of chloroform, in 60.2 of benzene. Petroleum ether, the volatile and fatty oils and glycerine, dissolve the alkaloid slightly, amyl alcohol freely ; it is insoluble in *anhydrous* ether. The behaviour of brucine in the subliming cell is described at p. 231. The alcoholic solution of brucine turns the plane of polarisation to the left $[a]r = -11.27^\circ$. The taste is bitter and acrid. Soubeiran maintains that it can be recognised if one part is dissolved in 500,000 parts of water. If nitric trioxide be passed into an alcoholic solution of brucine, first brucine nitrate is formed ; but this passes again into solution, from which, after a time, a heavy, granular, blood-red precipitate separates : it consists of dinitro-brucine ($C_{23}H_{24}(NO_3)_2N_2O_4$). Brucine fully neutralises acids, and forms salts which are for the most part crystalline. The neutral sulphate ($C_{23}H_{25}N_2O_4SH_2O_4 + 3\frac{1}{2}H_2O$) is in long needles, easily soluble in water. The acetate is not crystalline, that of strychnine is so (p. 291).

The precipitants of solutions of the salts of brucine are—ammonia, the caustic and carbonated alkalies, sulphocyanide of potash, platinic chloride, and a large number of general alkaloidal reagents.

Physiological Action.—No essential difference between the action of strychnine and that of brucine on man or animals has yet been demonstrated, save in a few minor points. To all intents and purposes speaking in a physiological sense, brucine is a diluted strychnine. The lethal-

* Methyl strychnine, as well as methyl brucine, has been shown by Brown and Fraser to have an effect exactly the opposite to that of strychnine, paralysing the muscles like curari. In the case, therefore, of the methyl compounds, a physiological test would be very valuable, since these compounds do not respond to the ordinary tests.

† Sonnenschein has asserted that brucine may be changed into strychnine by the action of NO_2 . This statement has been investigated by A. J. Cownley, but not confirmed.—*Pharm. Journ.* [3], vi., p. 841.

ity of brucine, especially as compared with strychnine, has been admirably investigated by F. A. Falck.* He experimented on eleven rabbits, injecting subcutaneously brucine nitrate, in doses of varying magnitude, from 100 mgrms. down to 20 mgrms. per kilogram of body-weight. He found that brucine presented three stages of symptoms. In the first the respiration is quickened ; in three of the eleven cases a strange injection of the ear was noticed ; during this period the pupils may be dilated. In the second stage there are tetanic convulsions; trismus, opisthotonus, oppressed respiration, and dilated pupils. In the third stage, the animal is moribund. Falck puts the minimum lethal dose for rabbits at 23 mgrms. per kilo. Strychnine kills 3·06 times more quickly than brucine, the intensity of the action of strychnine relative to that of brucine being as 1 : 117·4. Falck has also compared the minimum lethal dose of strychnine and brucine with the tetanising opium alkaloids, as shown in the following table :—

TABLE XIII.—LETHAL DOSES OF VARIOUS TETANISING POISONS.

	Minimum Lethal Dose for every Kilogram Weight of Rabbit.	Proportional Strength.
Strychnine Nitrate,	0·6	...
Thebaine Nitrate,	14·4	24·0
Brucine Nitrate,	23·0	38·33
Landanine Nitrate,	29·6	49·33
Codeine Nitrate,	51·2	85·33
Hydrocotarnine Nitrate,	203·8	339·66

If these views are correct, it follows that the least fatal dose for an adult man would be 1·84 grm. (about 13·4 grains of brucine nitrate).

Tests.—The best test of brucine is, in my opinion, the reaction with methyl iodide. If to a solution of brucine in strong alcohol a little methyl iodide is added, at the end of a few minutes circular rosettes of crystal groups appear (see fig 15) : they are composed of methyl brucine iodide ($C_{20}H_{28}(CH_3)N_2O_4HI$). Crystals identical in shape are also obtained if an alcoholic solution of iodine, or hydriodic acid with iodine is added to an alcoholic solution of brucine. A solution of strychnine gives

* *Brucin u. Strychnin; eine Toxicologische Parallele*, von Dr. F. A. Falck. *Vierteljahrsschr. f. Gerichtl. Med.*, Band xxiii., p. 78.

with methyl iodide no similar reaction. Strychnine in alcoholic solution, mixed with brucine, in no way interferes with the test. The methyl iodide test may be confirmed by the action of nitric acid. With that reagent it produces a scarlet colour, passing into blood-red, into yellow-red, and finally ending in yellow. This can be made something more than a mere colour test, for it is possible to obtain a crystalline body from the action of nitric acid on brucine. If a little of the latter be put in a test-tube, and treated with nitric acid of 1·4 specific gravity (immersing the test-tube in cold water to moderate the action), the red colour is produced. On spectroscopic examination of the blood-red liquid a broad, well-marked absorption band is seen, the centre of which is very near D.

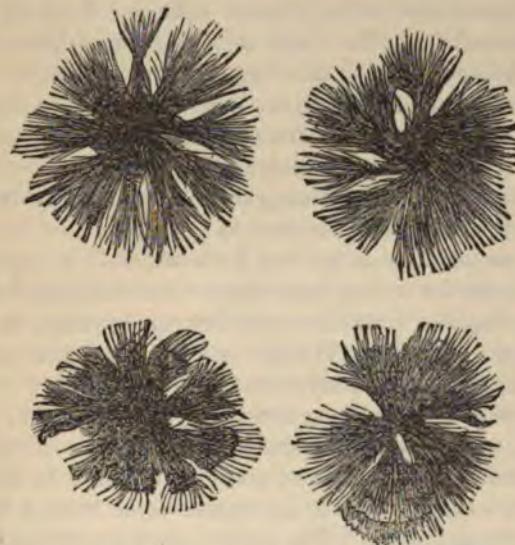


Fig. 15. (*From a Photograph.*)

[W. L. 589·4]. There is also a development of nitric oxide and carbon dioxide, and the formation of methyl nitrite, oxalic acid, and kakotelin ($C_{23}H_{26}N_2O_4 + 5NHO_3 = C_{20}H_{22}N_4O_9 + N(CH_3)O_2 + C_2H_2O_4 + 2NO + 2H_2O$). On diluting abundantly with water, the kakotelin separates in yellow flocks, and may be crystallised out of dilute hydrochloric or dilute nitric acid in the form of yellow or orange-red crystals, very insoluble in water, but dissolving readily in dilute acid. On removal by dilution of the product just named, neutralisation with ammonia, and addition of a solution of chloride of calcium, the oxalate of lime is thrown down. The nitric acid test is, therefore, a combined test, consisting of—the production by the action of nitric acid, (1) of a red colour; (2) of yellow scales

or crystals insoluble in water ; (3) of oxalic acid. No alkaloid save brucine is known to give this reaction.

There are other methods of producing the colour test. If a few drops of nitric acid are mixed with the substance in a test-tube, and then sulphuric acid cautiously added, so as to form a layer at the bottom, at the junction of the liquids, a red zone, passing into yellow, is seen.

A solution of brucine is also coloured red by chlorine gas, ammonia changing the colour into yellow.

Flückiger* has proposed as a test mercurous nitrate, in aqueous solution with a little free nitric acid. On adding this reagent to a solution of brucine salt, and gently warming, a fine carmine colour is developed.

In regard to the separation of brucine from organic fluids or tissues, the process already detailed for strychnine suffices. It is of very great importance to ascertain whether both strychnine and brucine are present or not—the presence of both pointing to *nux vomica* or one of its preparations. The presence of brucine may, of course, be owing to impure strychnine ; but if found in the tissues, that solution of the question is improbable, the commercial strychnine of the present day being usually pure, or at the most containing so small a quantity of brucine as would hardly be separated from the tissues.

Igasurine is an alkaloid as yet but little studied ; it appears that it can be obtained from the boiling hot watery extract of *nux vomica* seeds, through precipitating the strychnine and brucine by lime, and evaporation of the filtrate. According to Desnoix,† it forms white crystals containing 10 per cent. of water of crystallisation.

It is said to be poisonous, its action being similar to that of strychnine and brucine, and in activity standing midway between the two.

Strychnic Acid.—Pelletier and Caventou obtained by boiling with spirit small, hard, warty crystals of an organic acid, from *S. ignatius*, as well as from *nux vomica* seeds. The seeds were first exhausted by ether, the alcohol solution was filtered and evaporated, and the extract treated with water and magnesia, filtered, and the residue first washed with cold water, then with hot spirit, and boiled lastly with a considerable quantity of water. The solution thus obtained was precipitated with acetate of lead, the lead thrown out by SH_2 , and the solution evaporated, the acid crystallising out. It is a substance as yet imperfectly studied, and probably identical with malic acid.

* *Archiv. f. Pharm.*, [8], vi., 404.

† *Journ. Pharm.*, [8], xxv., 202.

2. THE QUEBRACHO GROUP OF ALKALOIDS.

The bark of the *Quebracho Blanco** (*Aspidosperma quebracho*) contains, according to Hesse's researches, no fewer than six alkaloids—Quebrachine, Aspidospermine, Aspidospermatine, Aspidosamine, and Hypoquebrachine. The more important of these are *Aspidospermine* and *Quebrachine*.

Aspidospermine ($C_{22}H_{30}N_2O_2$) forms colourless needles, which melt at 206° . They dissolve in about 6000 parts of water at 14° —48 parts of 90 per cent. alcohol, and 106 parts of pure ether. The alkaloid gives a fine magenta colour with perchloric acid.

Quebrachine ($C_{18}H_{28}N_2O_2$) crystallises in colourless needles, melting point (with partial decomposition), 215° . The crystals are soluble in chloroform, with difficulty soluble in cold alcohol, but easily in hot. The alkaloid, treated with sulphuric acid and peroxide of lead, strikes a beautiful blue colour. It also gives with sulphuric acid and potassic chromate the strychnine colours. Quebrachine, dissolved in sulphuric acid containing iron, becomes violet-blue, passing into brown. The alkaloid, treated with strong sulphuric acid, becomes brown; on adding a crystal of potassic nitrate, a blue colour is developed; on now neutralising with caustic soda, no red coloration is perceived. Dragendorff has recently studied the best method of extracting these alkaloids for toxicological purposes. He recommends extraction of the substances with sulphuric acid holding water, and shaking up with solvents. Aspidospermine is not extracted by petroleum ether or benzene from an acid watery extract, but readily by chloroform or by amyl alcohol. It is also separated from the same solution, alkalised by ammonia, by either amyl alcohol or chloroform; with difficulty by petroleum ether; some is dissolved by benzene. Quebrachine may be extracted from an acid solution by chloroform, but not by petroleum ether. Alkalised by ammonia it dissolves freely in chloroform and in amyl alcohol. Traces are taken up by petroleum, somewhat more by benzene. Aspidospermine is gradually decomposed in the body, but Quebrachine is more resistant, and has been found in the stomach, intestines, blood, and urine. The toxicological action of the bark ranks it with the tetanic class of poisons. In this country it does not seem likely to attain any importance as a poison.

3. PEREIRINE.

Pereirine.—An alkaloid from pereira bark, gives a play of colours with sulphuric acid and potassic bichromate similar to that of strychnine. Fröhde's reagent strikes with it a blue colour. On dissolving pereirine in dilute sulphuric

* See Liebig's *Annal.*, 211, 249-282; *Ber. der Deutsch. Gesellsch.*, 11, 2189; 12, 1560.

acid, and precipitating by gold chloride, the precipitate is a beautiful red, which, on standing and warming, is deepened. Pereirine may be extracted from an acid solution by benzene.

4. GELSEMINE.

Gelsemine is an alkaloid * which has been separated from *Gelsemium sempervirens*, the Carolina jessamine, a plant having affinities with several natural orders, and placed by De Candolle among the *loganiaceæ*, by Chapman among the *rubiaceæ*, and by Decaisne among the *apocynaceæ*. It grows wild in Virginia and Florida.† Gelsemine is a strong base ; it is yellowish when impure, but a white amorphous powder when pure. It fuses below 100° into a transparent vitreous mass, at higher temperatures it condenses on glass in minute drops ; its taste is extremely bitter ; it is soluble in 25 parts of ether, in chloroform, bisulphide of carbon, benzene, and in turpentine ; it is not very soluble in alcohol, and still less soluble in water, but it freely dissolves in acidulated water. The caustic alkalies precipitate it, the precipitate being insoluble in excess ; it is first white, but afterwards brick-red. Tannin, picric acid, iodised potassic iodide, platinic chloride, potassio-mercuric iodide, and mercuric chloride all give precipitates. Fröhde's reagent gives with gelsemine a brown changing to green.

Sulphuric acid dissolves gelsemine with a reddish or brownish colour ; after a time it assumes a pinkish hue, and if warmed on the water-bath, a more or less purple colour ; if a small crystal of potassic bichromate be slowly stirred in the sulphuric acid solution, reddish purple streaks are produced along the path of the crystal ; ceric oxide exhibits this better and more promptly, so small a quantity as .001 grain showing the reaction. This reaction is something like that of strychnine.

* Dr. T. G. Wormley separated, in 1870, a non-nitrogenised remarkably fluorescent body, which he named gelsemic acid (*Amer. Journ. of Pharm.* 1870), but Sonnenschein and C. Robbins afterwards found gelsemic acid to be identical with asculin (*Ber. der Deutsch. Chem. Ges.*, 1876, 1182). Dr. Wormley has, however, recently contested this, stating that there are differences. (*Amer. Journ. of Pharm.*, 1882, p. 337. "Yearbook of Pharmacy," 1882, p. 169).

† The following are its botanical characters :—Calyx five-parted, corolla funnel-shaped, five-lobed, somewhat oblique, the lobes almost equal, the posterior being innermost in bud ; stamens five ; anthers oblong saggitate, style long and slender ; stigmas two, each two parted, the divisions being linear ; fruit elliptical, flattened contrary to the narrow partition, two-celled, septically two-valved, the valves keeled ; seeds five to six in each cell, large, flat, and winged-embryo straight in fleshy albumen ; the ovate flat, cotyledons much shorter than the slender radicle ; stem smooth, twining and shrubby ; leaves opposite, entire, ovate, or lanceolate, shining on short petioles, nearly persistent ; flowers large, showy, very fragrant, yellow, one to five in the axil of the leaves.

nine, but nitric acid causes gelsemine to assume a brownish-green, quickly changing to a deep green—a reaction which readily distinguishes gelsemine from strychnine and other alkaloids.

Fatal Dose.—10 mgrms. killed a frog within four hours, and 8 mgrms. a cat within fifteen minutes. A healthy woman took an amount of concentrated tincture, which was equivalent to 11 mgrms. (6 grain), and died in seven and a half hours.

Effects on Animals—Physiological Action.—Gelsemine acts powerfully on the respiration; for example, Drs. Sydney Ringer and Murrell * found, on operating on the frog, that in two minutes the breathing had become distinctly slower; in three and a half minutes, it had been reduced by one-third; and in six minutes, by one-half; at the expiration of a quarter of an hour, it was only one-third of its original frequency; and in twenty minutes, it was so shallow and irregular that it could no longer be counted with accuracy. In all their experiments they found that the respiratory function was abolished before reflex and voluntary motion had become extinct. In several instances the animals could withdraw their legs when their toes were pinched, days after the most careful observations had failed to detect the existence of any respiratory movement. The heart was seen beating through the chest wall long after the complete abolition of respiration.

In their experiments on warm-blooded animals (cats), they noticed that in a few minutes the respirations were slowed down to twelve and even to eight, and there was loss of power of the posterior extremities, while at short intervals the upper half of the body was convulsed. In about half an hour paralysis of the hind limbs was almost complete, and the respiratory movements so shallow that they could not be counted. In the case of a dog, after all respiration had ceased, tracheotomy was performed, and air pumped in: the animal recovered.

Ringer and Murrell consider that gelsemine produces no primary quickening of the respiration, that it has no direct action on either the diaphragm or intercostal muscles, that it paralyses neither the phrenic nor the intercostal nerves, and that it diminishes the rate of respiration after both vagi have been divided. They do not consider that gelsemine acts on the cord through Setchenow's inhibitory centre, but that it destroys reflex power by its direct action on the cord, and that probably it has no influence on the motor nerves. Dr. Burdon Sanderson has also investigated the action of gelsemine on the respiration, more especially in relation to the movements of the diaphragm. He operated upon rabbits; the animal being narcotised by chloral, a small spatula, shaped like a teaspoon, was introduced into the peritoneal cavity through

* *Lancet*, vol. i., 1876, p. 415.

an opening in the linea alba, and passed upwards in front of the liver until its convex surface rested against the under side of the centrum tendineum. The stem of the spatula was brought into connection with a lever, by means of which its to-and-fro movements (and consequently that of the diaphragm) were inscribed. The first effect is to augment the depth but not the frequency of the respiratory movements; the next is to diminish the action of the diaphragm both in extent and frequency. This happens in accordance with the general principle applicable to most cases of toxic action—viz., that paresis of a central organ is preceded by over-action. The diminution of movement upon the whole is progressive, but this progression is interrupted, because the blood is becoming more and more venous, and therefore the phenomena of asphyxia are mixed up with the toxic effects. Dr. Sanderson concludes that the drug acts by paralysing the automatic respiratory centre; the process of extinction, which might be otherwise expected to be gradual and progressive, is prevented from being so by the intervention of disturbances of which the explanation is to be found in the imperfect arterialisation of the circulating blood. Ringer and Murrell have also experimented upon the action of gelsemine on the frog's heart. In all cases it decreased the number of beats; a small fatal dose produced a white contracted heart, a large fatal dose a dark dilated heart; in either case arrest of the circulation of course followed.

Effects on Man.—The preparations used in medicine are the fluid extract and the tincture of gelsemine; the latter appears to contain the resin of the root as well as the active principle. There are several cases on record of gelsemine, or the plant itself, having been taken with fatal effect.* Besides a marked effect on the respiration, there is an effect upon the eye, better seen in man than in the lower animals; the motor nerves of the eye are attacked first, objects cannot be fixed, apparently dodging their position, the eyelids become paralysed, droop, and cannot be raised by an effort of the will; the pupils are largely dilated, and at the same time a feeling of lightness has been complained of in the tongue; it ascends gradually to the roof of the mouth, and the pronunciation is slurred. There is some paresis of the extremities, and they refuse to support the body; the respiration becomes laboured, and the pulse rises in frequency to 120 or 130 beats per minute, but the mind remains clear. The symptoms occur in about an hour and a half after taking an over-dose of the drug, and, if not excessive, soon disappear, leaving no unpleasantness behind. If, on the other hand, the case proceeds to a fatal end, the respiratory trouble increases, and there may be

See *Lancet*, 1873, vol. ii., p. 475; *Brit. Med. and Surg. Journ.*, April, 1866; *Phil. Med. and Surg. Reporter*, 1861.

convulsions, and a course very similar to that seen in experimenting on animals. Large doses are especially likely to produce tetanus, which presents some clinical differences distinguishing it from strychnine tetanus. Gelsemine tetanus is always preceded by a loss of voluntary reflex power, respiration ceases before the onset of convulsions, the posterior extremities are most affected, and irritation fails to excite another paroxysm till the lapse of some seconds, as if the exhausted cord required time to renew its energy ; finally, the convulsions last only a short time.

Extraction from Organic Matters, or the Tissues of the Body.—Dragendorff states that, from as little as half a grain of the root, both gelsemine and gelsemic acid may be extracted with acid water, and identified. On extracting with water acidified with sulphuric acid, and shaking up the acid liquid with chloroform, the gelsemic acid (æsculin ?) is dissolved, and the gelsemine left in the liquid. The chloroform on evaporation leaves gelsemic acid in little micro-crystals ; it may be identified by (1) its crystallising in little tufts of crystals ; (2) its strong fluorescent properties, one part dissolved in 15,000,000 parts of water showing a marked fluorescence, which is increased by the addition of an alkali : and (3) by splitting up into sugar and another body on boiling with a mineral acid. After separation of gelsemic acid, the gelsemine is obtained by alkalising the liquid, and shaking up with fresh chloroform ; on separation of the chloroform, gelsemine may be identified by means of the reaction with nitric acid, and also the reaction with potassic bichromate and sulphuric acid.

V. THE ACONITE GROUP OF ALKALOIDS.

The officinal *aconite* is the *Aconitum napellus*—Monkshood or wolfs-bane—a very common garden plant in this country, and one cultivated for medicinal purposes. Many varieties of aconite exist in other regions which either are, or could be, imported. Of these the most important is the *Aconitum ferox*, a native of the Himalayan mountains, imported from India.

All the aconites, so far as known, are extremely poisonous, and it appears probable that different species contain different alkaloids. The root of *A. napellus* is from two to four inches long, conical in shape, brown externally and white internally. The leaves are completely divided at the base into five wedge-shaped lobes, each of the five lobes being again divided into three linear segments. The numerous seeds are

three-sided, irregularly twisted, wrinkled, of a dark-brown colour, in length one-sixth of an inch, and weighing 25 to the grain (*Guy*). The whole plant is one of great beauty, from two to six feet high, and having a terminal spike of conspicuous blue flowers. The root has been fatally mistaken for horse-radish—an error not easily accounted for, since no similarity exists between them.

Pharmaceutical Preparations of Aconite.—The preparations of aconite used in medicine are :—

Aconitine, officinal in all the pharmacopœias.

Aconite liniment (*Linimentum aconiti*), made from the root with spirit, and flavoured with camphor; officinal in the British pharmacopœia. It may contain about 2·0 per cent of aconitine.

Aconite tincture, officinal in all the pharmacopœias.

Aconite ointment, 8 grains to the ounce (*i.e.*, 1·66 per cent.); officinal in the British pharmacopœia.

Aconite extract, the juice of the leaves evaporated; officinal in most of the pharmacopœias.

Fleming's tincture of Aconite is not officinal, but is sold largely in commerce. It is from three to four times stronger than the P.B. tincture.

The Aconite Alkaloids.—The alkaloids which have been stated to exist in *A. napellus* are—Aconitine, napelline, aclyctine, lycocytine, and one or two others. The first is considered to be in combination with aconitic or equisetic acid ($H_3C_6H_3O_6$); the others are probably derivatives from aconitine, produced by the objectionable employment of mineral acids and too high a temperature in the process of extraction.

The researches of Dr. Adler Wright on the alkaloids contained in the aconites have thrown much light upon the subject, and are of the greatest importance. Only a summary of results as obtained by him can, of course, be given here, and the reader is referred to the original papers* for further information.

The alkaloids contained in *Aconitum napellus* are by no means identical with those contained in *Aconitum ferox*.

Aconitum napellus roots yield a crystallised alkaloid, *Aconitine* ($C_{33}H_{48}NO_{12}$), of great activity. Some roots, but apparently not all, contain in addition a nearly inert bitter base, termed by Dr. A. Wright, *Picraconitine* ($C_{31}H_{45}NO_{10}$). Besides picraconitine and aconitine, there is a third amorphous alkaloid, incapable of yielding crystalline salts, and of lower molecular weight.

Aconitum ferox contains an active alkaloid, to which Dr. Wright gives the name of *pseudaconitine*, and assigns the formula $C_{27}H_{37}NO_5$.

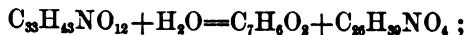
**Journ. Chem. Society*, i., 1877, p. 143; *ib. i.*, 1878, p. 151.

From pseudaconitine, apopseudaconitine ($C_{38}H_{47}NO_{11}$), pseudaconine ($C_{37}H_{41}NO_9$), apopseudaconine ($C_{37}H_{37}NO_8$), and other derivatives may be obtained.

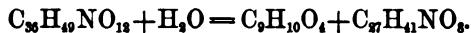
Confining our attention to the physiologically active alkaloids, *Aconitine* and *pseudaconitine*, the points of resemblance and difference between them are as follows:—They are both physiologically active, and both give precipitates with mercuric chloride, potassium mercurio-bromide, potassium mercuriiodide, tannin, gold chloride, and several other precipitants and alkaloids.

From aconitine, pseudaconitine differs in its molecular weight and in its melting point—aconitine melting at 189° , pseudaconitine at about 104° to 105° .

Aconitine by saponifying agents breaks up into benzoic acid and a new alkaloid, according to the reaction.



while pseudaconitine, treated similarly, gives rise to a new body (*pseudaconine*) and dimethyl-protocatechuic acid,



Aconitine, again, crystallises anhydrous; pseudaconitine with one atom of water. Aconitine yields well-crystallised salts with facility; pseudaconitine, treated similarly, produces amorphous varnishes, with a few exceptions—e.g., the nitrate.

Analysis of Pharmaceutical Preparations of Aconite.—The yield of total alkaloids from aconite roots is about 34 per cent. when Duquenne's process is used, but with the other methods the yield is very small—e.g., .002 per cent.—the heat destroying most of the alkaloid. The approximate strength of tinctures, liniments, &c., may be determined by Mayer's reagent.* Each cc. of this fluid precipitates .0269 of Duquenne's or Petit's aconitine. The titration, according to Dragendorff, must operate upon a fluid containing about one part of the alkaloid in 150 to 200 of water, and a first experiment is necessary in order to ascertain the proper degree of dilution. The reagent is then added from a burette, and by the use of a Beale's filter the point at which a precipitate ceases to be produced is noted.

Extracts of aconite must be treated with acidulated water, and filtered; spirituous preparations must be freed from alcohol, and acidulated. Herr Zinoffsky, operating in this way, found in Russian tinctures

* 13.546 grms. of mercuric chloride and 49.3 potassic iodide in a litre of water.

·116 to ·1 per cent. of aconitine. The alcoholic extracts appear to contain from 4 to 6·5 per cent.

Commercial aconitine may be assayed by the use of saponifying agents, changing aconitine and pseudaconitine respectively into benzoic and dimethyl-protocatechuic acids. The following is an example of this method :

0·7895 grain lost at 100° 0·0335,	= 4·2 per cent.
2·3040 grains, dissolved in hydrochloric acid, and treated with ether, furnished 0·010 grain of residue, left on spontaneous evaporation of ether, consisting of resinous matter with a little dimethyl-protocatechuic acid,	= 0·4 " "
2·0230 grains, heated from 240° to 250° in a sealed tube for twenty-four hours with water, yielded with hydrochloric acid and ether 0·3660 grain of mixed benzoic and dimethyl-protocatechuic acids, with trace of resin,	= 18·1 "
On distillation with water, 0·002 grm. of benzoic acid was obtained, melting at 110°	= 0·1 "

·1 per cent. of benzoic acid would correspond to 0·6 per cent. of aconitine, since pure aconitine has been found experimentally to yield about one-sixth of its weight of benzoic acid.

Pure pseudaconitine is assumed to yield 25 per cent. of its weight of dimethyl-protocatechuic acid; in other words, the percentage of dimethyl-protocatechuic acid multiplied by 4 (after making corrections for resin, pre-existing acid, and benzoic acid), equals for practical purposes the percentage of pseudaconitine. Hence the results of the previous analysis are thus worked out :—

Total dimethyl-protocatechuic and benzoic acids, and resin obtained,	= 18·1 per cent.
Deduct resin and pre-existing dimethyl-protocatechuic acid,	= 0·4 "
Acids due to pseudaconitine and aconitine present,	= 17·7 "
Benzoic acid due to aconitine,	= 0·1 "
Dimethyl-protocatechuic acid due to pseudaconitine,	= 17·6 "
Percentage of pseudaconitine,	= 17·6 × 4 = 70·4 "
Ditto of aconitine,	= 0·1 × 6 = 0·6 "
Water,	= 4·2 "

Pseudaconine and amorphous unnamed base, &c.,
by difference, — 24.8 per cent.

The various kinds of Commercial Aconitine and the Fatal Dose of Aconitine.—The commercial varieties of aconitine differ from each other in appearance and in quantitative action, but not, as the researches of Plugge prove, in qualitative action. The French aconitine nitrate of Petit is in white crystals, and is the purest of all and the most active. Morson's aconitine is pseudaconitine, a yellow-brown powder; it seems to approach, but not equal, Petit's in activity. Other aconitines are either brown or greyish powders—such, for example, as those of Merck and Friedländer—or transparent gummy masses, e.g., Hopkins & Williams' pseudaconitine. We possess, through the researches of Professor Plugge,* some very exact information as to the fatal dose (for the lower animals) of Petit's, Merck's and Friedländer's aconitine nitrate. He administered the following doses to the animals mentioned:—

TABLE XIV.—FATAL DOSES (FOR ANIMALS) OF ACONITINE.

PETIT'S CRYSTALLINE ACONITINE NITRATE.

Animals Experimented upon.	Dose Given.	Dose per Kilogram.	Result.
A Frog,4 mgrm.	16.0	Death in 60 Minutes.
A Rabbit,8 "	.5-.6	," 30. ,,
A Dog,	1.6 "	.21	," 20 ,,
"45 "	.10	," 140 ,,
"50 "	.054	Recovered.
"60 "	.075	Recovered.
A Pigeon,07 "	.22	Death in 21 Minutes.

* *Archiv der Pharm.*, Jan. 7, 1882. *Trans. of Internat. Med. Congress*, 1881, vol. i., p. 472.

MERCK'S ACONITINE NITRATE.

Animals Experimented upon.	Dose Given.	Dose per Kilogram.	Result.
A Frog,	4 mgm.	16	Recovered.
"	1.0 "	40	Died in 110-360 Min.
"	2.0 "	80	" 75-130 "
"	4.0 "	160	" 50 "
A Rabbit,	8.5 "	2	" 75 "
"	10 "	6.50	" 15 "
A Dog,	10 "	1.65	" 15 "
A Pigeon,	1.65	Recovered.

FRIEDLANDER'S ACONITINE NITRATE.

Animals Experimented upon.	Dose Given.	Dose per Kilogram.	Result.
A Frog,	4 mgrms.	160	Recovered.
"	10 "	400	
"	20 "	800	
"	40 "	1600	
A Rabbit,	6 "	4.11	Recovered.
"	24 "	18.00	"
"	50 "	85.50	"
A Dog,	28 "	6.00	"
A Pigeon,	10 "	33.4	"

The conclusions Plugge draws from his researches are that Petit's aconitine is at least eight times stronger than that of Merck, and seventy times more toxic than that of Friedländer, while Merck's "aconitine again is twenty to thirty times stronger than Friedländer's." He is inclined to put seven commercial samples which he has examined in the following diminishing order of toxicity:—(1) Petit's crystalline aconitine nitrate; (2) Morson's aconitine nitrate; (3) Hottot's aconi-

tine nitrate; (4) Hopkins & Williams' pseudoaconitine; (5) Merck's aconitine nitrate; (6) Schuchart's aconitine sulphate; and (7) Friedländer's aconitine nitrate.

From a study of Dr. Harley's experiments,* however, made a few years ago, I take it that there is very little difference between the activity of Petit's and Morson's aconitine. Dr. Harley experimented on a young cat, 3 lbs. in weight, and nearly killed it with $\frac{1}{1000}$ of a grain of Morson's aconitine; two other cats, also weighing 3 lbs. each, died in seven and a half hours and three quarters of an hour respectively, killed from a subcutaneous dose of $\frac{1}{50}$ of a grain. Reducing these values to the ordinary equivalents, the dose, after which the cat recovered with difficulty, is equal to about .048 mgrm. per kilo., while a certainly fatal dose is .092 mgrm. per kilo., therefore, it seems likely that the least fatal dose for Morson's, as for Petit's, is some number between .075 and .09 mgrm. per kilo.

Man is evidently more sensitive to aconitine than any of the dogs or cats experimented upon, since, in the German cases to be recorded, 1.6 mgrm. of Petit's aconitine nitrate, taken by the mouth, gave rise to symptoms so violent that it was evidently a dangerous dose, while 4 mgrms. were rapidly fatal; but if man took the same amount per kilo. as dogs or cats, he would require a little over 6 mgrms. to be certainly fatal. It seems to me, from the evidence obtainable, that .03 grain (2 mgrms.) is about the least fatal dose for an adult man of standard weight. This dose is equal to .028 mgrm. per kilo., and, of course, refers either to Morson's aconitine or French aconitine, the alkaloid being taken by the mouth. If given by subcutaneous injection, probably 1.5 mgrm. would kill, for the whole of the poison is then thrown on the circulation at one time; and there is no chance of its elimination by vomiting.

The lethal dose of the pure alkaloid being even approximatively settled, it is possible to get a more exact idea as to the suitable medicinal dose of the tincture and extract, and also to study more profitable the "quantitative toxicity." The English officinal tincture, although variable in strength, may for our purposes be regarded as averaging 1 per cent. of alkaloid—that is, in every 100 parts by volume there will be 1 part of the alkaloid by weight, and Fleming's tincture may be considered as one-third stronger, containing in every 100 parts .13 part of alkaloid. The medicinal dose of the P.B. tincture is laid down as from 5 to 15 min.—equal to .005 to .015 grain of aconitine. The German pharmacopœia gives the maximum single dose as 1 cc. (say 15 mins.), and the maximum quantity to be taken in the twenty-four hours as four times that quantity. As before stated, 2 mgrms. (.030 grain) of aconitine being consid-

* "On the Action and Use of Aconitine," *St. Thos. Hosp. Report*, 1874.

ered a fatal dose, this is equivalent to about 2 cc. (30 minis.) of the P.B. tincture, or to 1·2 cc. (20 mins.) of Fleming's tincture in a single dose; and on these theoretical grounds I should consider this dose dangerous, and in the absence of prompt treatment likely to be fatal to an adult man. The usual least fatal dose laid down in medical toxicological works, however, is greater than this—viz., 3·75 cc. (a drachm).

In 1863, a woman took 70 minims of Fleming's tincture, and a grain of acetate of morphine, and died in about four hours; but as this was a complex case of poisoning, it is not of much value. Fifteen minims of the tincture caused very serious symptoms in the case of a woman under the care of Dr. Topham,* the effects lasting many hours. Probably the smallest quantity of the tincture recorded as having destroyed life is in the case of Dr. Male, of Birmingham.† He died from the effects of eighty drops taken in ten doses, extending over a period of four days—the largest dose at any one time being ten drops, the total quantity would perhaps equal ·08 grain of aconitine.

The P.B. extract is not a very satisfactory preparation, varying much in strength. It may be taken to average about ·6 per cent., and if so, applying the same reasoning as before, from ·26 to ·32 grm. (4 to 5 grains) would be a fatal dose.‡ On the other hand, there is an alcoholic extract which is very powerful, and averages 5 per cent. of aconitine: 40 mgrms. (·6 grain) of this extract would be likely to be fatal. With regard to the root itself, 3·8 grms. (60 grains) have been known to produce death, and from the average alkaloidal contents it is probable that ·648 grm. (10 grains) would be a highly dangerous dose.

Effects of Aconitine on Animal Life.—There are few substances which have been experimented upon in such a variety of ways and upon so many classes of animals, as aconitine in different forms: but there does not seem to be any essential difference in the symptoms produced in different animals, save that which is explained by the organisation of the life-form under experiment.

Insects.—I have recently made many experiments with the active principles of aconite upon blow-flies. An extract was made by allowing the ordinary tincture to evaporate spontaneously at the temperature of the atmosphere. If a minute dot of this was placed upon the head of a

* *Lancet*, July 19, 1851, p. 56.

† *Med. Gaz.*, vol. xxxvi, p. 861, quoted by Taylor, *Prin. of Med. Juris.*, vol. i. p. 426.

‡ But there is a case reported by Dr. Vachell, of Cardiff, in which 2 grains of extract of aconite taken in pills proved fatal. Now 2 grains is the medicinal dose, laid down as a maximum in the pharmacopeia; a complete revolution is, therefore, necessary in the use of these active remedies. No extract or tincture should be used until its approximate strength in active principles is determined.

blow-fly, absorption of the active principle would take place in from fifteen to thirty minutes, and very marked symptoms would result. They consisted essentially of muscular weakness, inability to fly, and to walk up perpendicular surfaces ; there was also in all cases a curious entanglement of the legs, and very often extrusion of the proboscis ; trembling of the legs and muscular twitchings were also frequent. A progressive paralysis terminated in from four to five hours in death ; the death was generally so gradual that it was difficult to know when the event occurred, but in one case there were violent movements of the body, and sudden death.*†

Fish.—The action on fish has been studied by Schulz and Praag.

* The more important physiological researches on the action of aconite are contained in the following works and papers :—

FLEMING, A.—“An inquiry into the physiological and medicinal properties of the *Aconitum napellus*,” to which are added observations on several other species of aconite. 8vo. Lond., 1845.

SCHULZ, F. W.—*De Aconitini Effectu in Organismum Animalum.*

V. PRAGG.—*Arch. f. Path. Anat.*, vii., p. 498, 1854.

HOTTOT, E.—*De l'Aconitine et de ses Effets Physiologiques*, 4to. Paris, 1863.

ACHSCHARUMOW.—*Arch. f. Anatom. u. Physiol.*, 1866.

BÖHN.—*Herzgifte*, 1871.

EWERS, C.—*Ueber die physiologischen Wirkungen des aus Aconitum ferox dargestellten Aconitins (Pseudoaconitin, Aconitum anglicum, Nepalin)*. 8vo. Dorpat, 1873.

GUILLAUD.—*De l'Aconite et de l'Aconitine*. 4to. Montpellier, 1874.

FRANCESCHINI, M. A.—*Contribution à l'Etude de l'Action Physiologique et Thérapeutique de l'Aconitine*. 4to. Paris, 1875.

LEWIN.—*Exp. Untersuch. über die Wirkung d. Aconitins auf's Herz. Diss.* Berlin, 1875.

GIULINI, P.—*Experimentelle Untersuchungen ueber die Wirkung des Aconitins auf das Nervensystem, das Herz, u. die Athmung*. 8vo. Erlangen, 1876.

HARLEY, DR. JOHN.—On the action and uses of Aconitum. St. Thos. Hosp. Reports, 1874.

V. SCHROFF, C. Jr.—*Beitrag zur Kenntniss des Aconit*. 8vo. Wien, 1876.

PLUGGE, P. C.—*Untersuchungen ueber die physiologische Wirkung verschiedener Handelssorten von Aconitin, u. Pseudoaconitin auf Muskeln u. Nerven*. *Virch. Archiv*, Bd. 87, 1882; S. 410.

† It may be well to quote in full a typical experiment. Six P.M., a little extract smeared on the head of a blow-fly. Forty-five minutes after—makes no attempt to fly, great muscular weakness, no trembling or convulsive movements. Fifty minutes after—partial paralysis of right half of body, so that the fly, on moving, goes in a circular direction, the second pair of legs are curiously bent forward and useless ; the wings seem fairly strong. Seventy-five minutes—fly very dull, always in one spot, without movement ; when placed on a horizontal glass surface, and the glass then very slowly inclined, until it is at last quite perpendicular, the fly falls. There is now a strange entanglement of the legs. 125 minutes—perfectly paralysed ; 145 minutes—dead.

There is rapid loss of power and diminished breathing ; the respiration seems difficult, and the fish rapidly die.

Reptiles—Frogs.—The most recent experiment on frogs are those of Plugge, and although his interpretation of the phenomena in some points is different from that of previous observers, the symptoms themselves are, as might have been expected, not different from those described by Achscharumow, L. v. Praag, and others. As before mentioned, Plugge found no qualitative difference in the action of any of the commercial samples of aconitine. This fact gives the necessary value to all the old experiments, for we now know that, although they were performed with impure or weak preparations, yet there is no reason to believe that the symptoms described were due to any other but the alkaloid aconitine in varying degrees of purity or dilution. Frogs show very quickly signs of weakness in the muscular power ; the respiration invariably becomes laboured, and ceases after a few minutes ; the heart's action becomes slowed, irregular, and then stops in diastole. The poisoned heart, while still pulsating, cannot be arrested either by electrical stimulation of the vagus or by irritation of the sinus, nor when once arrested can any further contraction be excited in it. Opening of the mouth and apparent efforts to vomit, Plugge observed both with *Rana esculenta* and *Rana temporaria*. He considers them almost invariable signs of aconitine poisoning. A separation of mucous from the surface of the body of the frog is also very constantly observed. Dilatation of the pupils is frequent, but not constant ; there may be convulsions, both of a clonic and tonic character before death, but fibrillar twitchings are seldom. (With regard to the dose required to affect frogs, see *ante*, pp. 319 and 320).

Birds.—There is a discrepancy in the descriptions of the action of aconitine on birds. L. v. Praag thought the respiration and circulation but little affected at first ; while Achscharumow witnessed in pigeons dyspnoea, dilatation of the pupils, vomiting, shivering, and paresis. It may be taken that the usual symptoms observed are some difficulty in breathing, a diminution of temperature, a loss of muscular power generally (but not constantly), dilatation of the pupils, and convulsions before death.

Mammals.—The effects vary somewhat according to the dose. Very large doses kill rabbits rapidly. They fall on their sides, are violently convulsed, and die in an asphyxiated condition ; but with smaller doses the phenomena first observed are generally to be referred to the respiration. Thus, in an experiment on the horse, Dr. Harley found that the subcutaneous administration of '6 mgrm. ('01 grain) caused in a weakly colt some acceleration of the pulse and a partial paralysis of the dilator narium. Double the quantity given to the same animal some time after, caused, in six hours and a half, some muscular weakness and an evident

respiratory trouble. The horse recovered in eighteen hours. 2·7 mgrms. ($\frac{1}{4}$ grain) given in the same way, after a long interval of time, caused, at the end of an hour, more pronounced symptoms ; the pulse, at the commencement 50, rose in an hour and a half to 68, then the respiration became audible and difficult. In an hour and three quarters there were great restlessness and diminution of muscular power. Two hours after the injection the muscular weakness increased so much that the horse fell down ; he was also convulsed. After eight hours he began to improve. In another experiment, 32·4 mgrms. ($\frac{1}{2}$ grain) killed a sturdy entire horse in two hours and twenty minutes, the symptoms commencing within the hour, and consisting of difficulty of breathing, irregularity of the heart's action, and convulsions.

The general picture of the effects of fatal, but not excessive, doses given to dogs, cats, rabbits, &c., resembles closely that already described. The heart's action is at first slowed, then becomes quick and irregular, there is dyspnoea, progressive paralysis of the muscular power, convulsions, and death in asphyxia. Vomiting is frequently observed, sometimes salivation, and very often dilatation of the pupil. Sometimes the latter is abnormally active, dilating and contracting alternately. Diarrhoea also occurs in a few cases. Vomiting is more frequent when the poison is taken by the mouth than when administered subcutaneously.

Effects on Man.—I have collected from European Medical literature, of the last ten years, 87 cases of poisoning by aconite in some form or other. These comprise only 2 cases of murder, 7 of suicide, and 7, which were more or less accidental. Six of the cases were from the use of the alkaloid itself ; 10 were from the root ; in 2 cases children ate the flowers ; in 1, the leaves of the plant were cooked and eaten by mistake ; in 7, the tincture was mistaken for brandy, sherry, or liqueur ; the remainder were caused by the tincture, the liniment, or the extract.

Poisoning by the Root.—A case of murder which occurred some years ago in America, and also the Irish case which took place in 1841 (*Reg. v. M'Conkey*), were, until the recent trial of Lamson, the only instances among English-speaking people of the use of aconite for criminal purposes ; but if we turn to the Indian records, we find that it has been largely used from the earliest times as a destroyer of human life. In 1842 a tank of water destined for the use of the British army in pursuit of the retreating Burmese, was poisoned by intentional contamination with the bruised root of *Aconitum ferox* ; it was fortunately discovered before any harm resulted. A preparation of the root is used in all the hill-districts of India to poison arrows for the destruction of wild beasts. A Lepcha described the root to a British officer as being “useful to sportsmen for destroying elephants and tigers, useful to the rich for putting troublesome relations out of the way, and useful to jealous husbands

for the purpose of destroying faithless wives." From the recorded cases, the powdered root, mixed with food, or the same substance steeped in spirituous liquor, is usually the part chosen for administration. In M'Conkey's case, the man's wife purchased powdered aconite root, mixed it with pepper, and strewed it over some greens, which she cooked and gave to him. The man complained of the sharp taste of the greens, and soon after the meal vomited and suffered from purging, became delirious with lock-jaw, and clenching of the hands; he died in about three hours. The chief noticeable *post-mortem* appearance was a bright red colour of the mucous membrane of the stomach.

The symptoms in this case were, in some respects, different from those met with in other cases of poisoning by the root. A typical case is given by Dr. Chevers (*Op. cit.*), in which a man had taken by mistake a small portion of aconite root. Immediately after chewing it he felt a sweetish taste, followed immediately by tingling of the lips and tongue, numbness of the face, and severe vomiting. On admission to hospital he was extremely restless, tossing his limbs about in all directions and constantly changing his position. He complained of a burning sensation in the stomach, and a tingling and numbness in every part of the body, excepting his legs. The tingling was specially marked in the face and tongue—so much so that he was constantly moving the latter to and fro in order to scratch it against the teeth. Retching and vomiting occurred almost incessantly, and he constantly placed his hand over the cardiac region. His face was anxious, the eyes suffused, the lips pale and exsanguine, the eye-lids swollen, moderately dilated, and insensible to the stimulus of light; the respiration was laboured, 64 in a minute; the pulse 66, small and feeble. There was inability to walk from loss of muscular power, but the man was perfectly conscious. The stomach-pump was used, and albumen and milk administered. Three and three quarter hours after taking the root the symptoms were increased in severity. The tongue was red and swollen, the pulse intermittent, feeble, and slower. The tingling and numbness had extended to the legs. On examining the condition of the external sensibility with a pair of scissors, it was found that, on fully separating the blades and bringing the points in contact with the skin over the arms and forearms, he felt them as one, although they were 4 inches apart. But the sensibility of the thighs and legs was less obtuse, for he could feel the two points distinctly when they were 4 inches apart, and continued to do so until the distance between the points fell short of $2\frac{3}{4}$ inches. He began to improve about the ninth hour, and gradually recovered, although he suffered for one or two days from a slight diarrhoea. As in the case detailed (p. 327), no water was passed for a long time, as if the bladder early lost its power.

Poisoning by the Alkaloid Aconitine.—Probably the earliest instance

on record is the case related by Dr. Golding Bird in 1848.* What kind of aconitine was then in commerce I know not, and since apparently a person of considerable social rank was the subject of the poisoning, the case has been imperfectly reported. It seems, however, that, whether for purposes of suicide, or experiment, or as a medicine, two grains and a half of aconitine were swallowed. The symptoms were very violent, consisting of vomiting, collapse, and attacks of muscular spasm ; the narrator describes the vomiting as peculiar. "It, perhaps, hardly deserved that title ; the patient was seized with a kind of general spasm, during which he convulsively turned upon his abdomen, and with an intense contraction of the abdominal muscles, he jerked out, as it were, with a loud shout, the contents of his stomach, dependent apparently on the sudden contraction of the diaphragm." On attempting to make him swallow any fluid, a fearful spasm of the throat was produced ; it reminded his medical attendants of hydrophobia. The patient recovered completely within twenty-four hours.

One of three cases reported by Dr. Albert Busscher,† of poisoning by aconitine nitrate, possesses all the exact details of an intentional experiment, and is of permanent value to toxicological literature.

A labourer of Beerta, sixty-one years of age, thin, and of somewhat weak constitution, suffered from neuralgia and a slight intermittent fever ; Dr. Carl Meyer prescribed for his ailment :—

R. Aconiti Nitrici, 2 grm.

Tr. Chenopodii Ambrosioid, 100 grms. M.D.S.

Twenty drops to be taken four times daily. The patient was instructed verbally by Dr. Meyer to increase the dose until he attained the maximum of sixty drops per day.

The doses which the man actually took, and the time of taking them, are conveniently thrown into a tabular form as follows :—

No. 1.	March 14,	7 P. M.	10 drops equal to aconitine nitrate,	4 mgrm.	
.. 2.		9 P. M.	20	"	1·7 "
.. 3.	March 15,	8 A. M.	20	"	1·6 "
.. 4.		11 A. M.	20	"	1·6 "
.. 5.		4 P. M.	20	"	1·6 "
.. 6.		9 P. M.	20	"	1·6 "
.. 7.	March 16,	10 P. M.	10	"	·8 "

In the whole seven doses, which were distributed over forty-eight hours, he took 9·2 mgrms. (·14 grain) of aconitine nitrate.

On taking dose No. 1, he experienced a feeling of constriction (*Zus-*

* *Lancet*, vol. i., p. 14.

† *Intoxicationsfälle durch Aconitin Nibricum Gallicum, nebst Sections Bericht.* von Dr. Albert Busscher ; *Berl Klinische Wochenschrift*, 1880, No. 24, pp. 338, 356

ammenziehung), and burning spreading from the mouth to the stomach, but this after a little while subsided. Two hours afterwards he took No. 2, four times the quantity of No. 1. This produced the same immediate symptoms, but soon he became cold, and felt very ill. He had an anxious oppressive feeling about the chest, with a burning feeling about the throat ; the whole body was covered with a cold sweat, his sight failed, he became giddy, there was excessive muscular weakness, he felt as if he had lost power over his limbs, he had great difficulty in breathing. During the night he passed no water, nor felt a desire to do so. About half an hour after he had taken the medicine, he began to vomit violently, which relieved him much ; he then fell asleep.

Dose No. 3, equal as before to 1·6 mgrm., he took in the morning. He experienced almost exactly the same symptoms as before, but convulsions were added, especially of the face ; the eyes were also prominent ; twenty minutes after he had taken the dose, vomiting came on, after which he again felt better.

He took dose No. 4, and had the same repetition of symptoms, but in the interval between the doses he felt weaker and weaker ; he had no energy, and felt as if paralysed. No. 5 was taken, and produced, like the others, vomiting, after which he felt relieved. Neither he nor his wife seemed all this time to have had any suspicion that the medicine was really doing harm, but thought that the effects were due to its constant rejection by vomiting, so, in order to prevent vomiting with No. 6, he drank much cold water. After thus taking the medicine, the patient seemed to fall into a kind of slumber, with great restlessness ; about an hour and a half afterwards he cried, "I am chilled ; my heart, my heart is terribly cold. I am dying ; I am poisoned." His whole body was covered with perspiration ; he was now convulsed, and lost sight and hearing ; his eyes were shut, his lips cracked and dry, he could scarcely open his mouth, and he was extremely cold, and thought he was dying. The breathing was difficult and rattling ; from time to time the muscular spasms came on. His wife now made a large quantity of hot strong black tea, which she got him to drink with great difficulty ; although it was hot, he did not know whether it was hot or cold. About five minutes afterwards he vomited, and did so several times ; this apparently relieved him, and he sank into a quiet sleep ; during the night he did not urinate. In the morning the wife went to Dr. Carl Meyer, described the symptoms, and accused the medicine. So convinced was Dr. Meyer that the medicine did not cause the symptoms, that he poured out a quantity of the same, equal to 4 mgrms. of aconitine nitrate, and took it himself in some wine, to show that it was harmless, and ordered them to go on with it. The unhappy physician died of aconitine poisoning five hours after taking the

medicine.* In the meantime, the woman went home, and her husband actually took a seventh, but smaller dose, which produced similar symptoms to the former, but of little severity; no more was taken.

The absence of diarrhoea, and of the pricking sensations so often described, is in this case noteworthy. Both diarrhoea and formication were also absent in a third case reported by Dr. Busscher in the same paper.

The facts of the following recent case are still fresh in public memory:—At the Central Criminal Court, in March, 1882, George Henry Lamson, surgeon, was convicted of the murder of his brother-in-law, Percy Malcolm John. The victim was a weakly youth of eighteen years of age, paralysed in his lower limbs from old standing spinal disease. The motive for perpetrating the crime was that Lamson, through his wife (Malcolm John's sister), would receive on the death of his brother-in-law a sum of £1,500, and, according to the evidence, it is probable that there had been one or more previous attempts by Lamson on the life of the youth with aconitine given in pills and in powders. However this may be, on Nov. 24, 1880, Lamson purchased 2 grains of aconitine, came down on Dec. 3 to the school where the lad was placed, had an interview with his brother-in-law, and, in the presence of the head-master, gave Malcolm John a capsule, which he filled then and there with some white powder, presumed at the time to be sugar. Lamson only stayed altogether twenty minutes in the house, and directly after he saw his brother-in-law swallow the capsule, he left. Within fifteen minutes Malcolm John became unwell, saying that he felt as if he had an attack of heart-burn, and then that he felt the same as when his brother-in-law had on a former occasion given him a quinine pill. Violent vomiting soon set in, and he complained of pains in his stomach, a sense of constriction in his throat, and of being unable to swallow. He was very restless—so much so that he had to be restrained by force from injuring himself. There was delirium a few minutes before death, which took place about three hours and three quarters after swallowing the fatal dose. The *post-mortem* appearances essentially consisted of redness of the greater curvature of the stomach, and the posterior portion of the same organ. In one part there was a little pit, as if a blister had broken; the rest of the viscera were congested, and the brain also slightly congested.†

*The symptoms suffered by Dr. Meyer are to be found in *Neder Tijdschrift van Geneskunde*, 1880, No. 16.

† To these cases of poisoning by the alkaloid aconitine may be added one recorded in Bouchardat's *Annuaire de Thérapeutie*, 1881, p. 276. The case in itself is of but little importance, save to illustrate the great danger in permitting the dispensing of such active remedies of varying strength. A gentleman, suffering from "angina pectoris," was prescribed "Hottot's aconitine" in granules, and directed carefully to increase the dose up to four granules, according to the effect

The symptoms of poisoning by the tincture, extract, and other preparation, do not differ from those detailed. As unusual effects, occasionally seen, may be noted profound unconsciousness lasting for two hours (Topham's case), violent twitching of the muscles of the face, opisthotonus, and violent convulsions. It is important to distinguish the symptoms which are not constant from those which are constant, or nearly so. The tingling and creeping sensations about the tongue, throat, lips, &c., are not constant ; they certainly were not present in the remarkable German case cited at p. 327. Speaking generally, they seem more likely to occur after taking the root or the ordinary medicinal preparations. A dilated state of the pupil is by no means constant, and not to be relied upon. Diarrhoea is seen after taking the root or tincture by the stomach, but is often absent. In short, the only constant symptoms are difficulty of breathing, progressive muscular weakness, generally vomiting, and a weak intermittent pulse.

Physiological Action.—Aconitine, according to Dr. S. Ringer, is a protoplasmic poison, destroying the functions of all nitrogenous tissue—first of the central nervous system, next of the nerves, and last of the muscles. Aconitine without doubt acts powerfully on the heart, ultimately paralysing it ; there is first a slowing of the pulse, ascribed to a central excitation of the vagus, then quickening due to paralysis of the peripheral termination of the vagus in the heart ; lastly, the heart's action becomes slow, irregular, and weak, and the blood-pressure sinks. The dyspnoea and convulsions are the usual result, seen among all warm-blooded animals, of the heart affection. Plugge found that the motor nerves, and more especially their intra-muscular terminations, were always paralysed ; but if the dose was small the paralysis might be incomplete. Bœhm and Wartmann, on the other hand, considered that the motor paralysis had a central origin, a view not supported by recent research. The action of aconitine in this way resembles curare. The muscles themselves preserve their irritability, even after doses of aconitine which are five to ten times larger than those by which the nerve terminations are paralysed.

Post-mortem Appearances.—Among animals (mammals) the appearances most constantly observed have been hyperæmia of the cerebrum produced. The prescription was taken to a pharmacist, who, instead of supplying Hottot's aconitine, supplied some other of unknown origin. The medicine was taken daily, and the dose raised to four granules, which were taken with benefit until the whole was exhausted. He then went to Hottot's establishment, and had a fresh supply, presumably of the same substance, but a very little time after he had taken his usual dose of four granules, he suffered from symptoms of aconitine poisoning, headache, vertigo, feebleness of the voice, and muscular weakness, and was alarmingly ill. He recovered after some hours of medical treatment.

bral membranes and brain, a fulness of the large veins, the blood generally fluid—sometimes hyperæmia of the liver, sometimes not. When aconitine has been administered subcutaneously, there have been no inflammatory appearance in the stomach and bowels.

In case of Dr. Carl Meyer, who died in five hours from swallowing 4 mgrms. of aconitine nitrate, the corpse was of a marble paleness, the pupils moderately dilated. The colour of the large intestine was pale ; the duodenum was much congested, the congestion being most intense the nearer to the stomach ; the mucous membrane of the stomach itself was strongly hyperæmic, being of an intense red colour ; the spleen was enlarged, filled with much dark blood. The liver and kidneys were deeply congested, the lungs also congested ; the right ventricle of the heart was distended with blood ; in the pericardium there was a quantity of bloody serum. The brain was generally blood-red ; in the cerebral hemispheres there were several large circumscribed subarachnoid extravasations. The substance of the brain on section showed many red bloody points.

In a case recorded by Taylor, in which a man died in three hours from eating a small quantity of aconitine root, the only morbid appearance found was a slight reddish-brown patching the cardiac end of the stomach, of the size of half a crown ; all the other organs being healthy.

Separation of the Aconite Alkaloids.—It would appear certain that in all operations for the separation of aconite alkaloids (whether from the organic matters which make up the plant, or from those constituting animal tissues), mineral acids and a high heat should be avoided. A modification of M. Duquesnel's process of isolation is best—viz., extraction by alcohol, feebly acidulated with tartaric acid ; evaporation of the extract at temperatures not exceeding 60° ; re-solution of the extract in water ; agitation of the acid liquid with ether to remove impurities ; and finally, precipitation by sodium bicarbonate. Any precipitate should be crystallised, if possible, several times from ether and petroleum, and lastly, converted into an acid oxalate, and regenerated from the oxalate by reprecipitation with carbonate of soda ; or, if the alkaloid sought is derived from *A. ferox*, the purification appears best affected by conversion of pseudaconitine into nitrate (the nitrate of pseudaconitine is almost insoluble in nitric acid containing 8 to 10 per cent. of HNO₃), and from the nitrate the alkaloid may be regenerated by sodic carbonate.

In this way it is possible (should any of the preparations of aconite, or the root itself, have been taken) to isolate a more or less minute portion of an alkaloid, which, if applied to the skin, causes local anaesthesia. If a minute quantity is rubbed on the lip, or placed on the tongue, it will cause tingling and numbness. In order to be personally ac-

quainted with this feeling, the tincture (or the liniment of aconite) can be tried in the same way, and the sensations compared.

The chemical examination in the Lamson case was entrusted to Dr. Stevenson, assisted by Dr. Dupré, and was conducted on the principles detailed. The contents of the stomach were treated with alcohol, and digested at the ordinary temperature of the atmosphere; the contents were already acid, so no acid in this first operation was added. The mixture stood for two days and was then filtered. The insoluble portion was now exhausted by alcohol, faintly acidulated by tartaric acid, and warmed to 60°; cooled and filtered, the insoluble part being washed again with alcohol. The two portions—that is, the spirituous extract acid from acids preexisting in the contents of the stomach, and the alcohol acidified by tartaric acid—were evaporated down separately, and then were exhausted by absolute alcohol, the solutions filtered and dissolved in water. The two aqueous solutions were now mixed, and shaken up with ether, which, as the solution was acid, would not remove any alkaloid, but might remove various impurities; the residue, after being thus partially purified by ether, was alkalinised by sodic carbonate and the alkaloid extracted by a mixture of chloroform and ether. On evaporation of the chloroform and ether, the resulting extract was tested physiologically by tasting, and also by injections into mice. By means analogous to those detailed, the experts isolated aconitine from the vomit, the stomach, liver, spleen, and urine, and also a minute quantity of morphine, which had been administered to the patient to subdue the pain during his fatal attack. When tasted, the peculiar numbing, tingling sensation lasted many hours. These extracts were relied upon as evidence, for their physiological effect was identical with that produced by aconitine. For example, the extract obtained from the urine caused symptoms to commence in a mouse in two minutes, and death in thirty minutes, and the symptoms observed by injecting a mouse with known aconitine, coincided in every particular with the symptoms produced by the extraction from the urine.

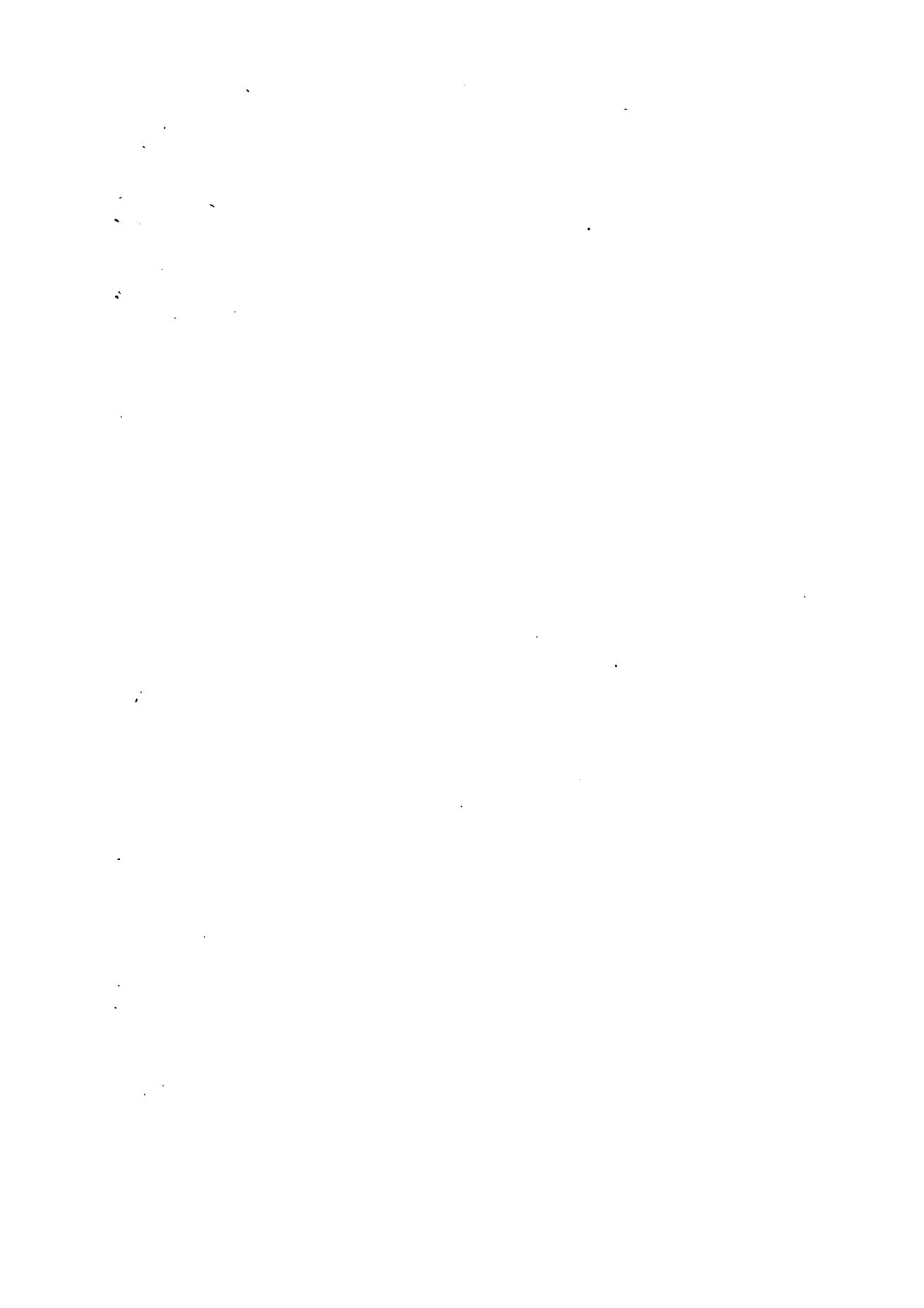
In our present state of knowledge, the identification of the active principle of the aconites must rest almost entirely upon physiological evidence, for though the substance must be isolated and identified as an alkaloid, yet the chemical tests (such as that it strikes a red colour with sugar and sulphuric acid, and a violet when stirred up with some drops of syrupy phosphoric acid, and heated for fifteen minutes on the water-bath) are not to be relied upon. If they were, they are deficient in delicacy. J. H. Munro * poisoned a sparrow with 1 grain of aconite root; it died within an hour; nearly all the root was found in the gizzard, very little being left in the crop. The contents of the crop and

* *Chem. News.*, vol. xlvi., p. 110.

gizzard were mixed, and a separation of the alkaloid was attempted quite in the manner recommended above. The ultimate extract dissolved in a few drops of water, did not respond either to the taste or to any chemical test ; yet some bread-crumbs soaked in the solution, and administered to a tom-tit, killed the bird within two or three hours.

With regard to the manner of using "life tests," since in most cases extremely small quantities of the active principle will have to be identified, the choice is limited to small animals, and it is better to use mice or birds, rather than reptiles. In the Lamson case, subcutaneous injections were employed, but it is a question whether there is not less error in administering it by the mouth. If two healthy mice are taken, and the one fed with a little meal, to which a weighed quantity of the extract under experiment has been added, while to the other some meal mixed with a supposed equal dose of aconitine is given, then the symptoms may be compared ; and several objections to any operative proceeding on such small animals are obviated. It is certain that any extract which causes distinct numbness of the lips will contain enough of the poison to kill a small bird or a mouse if administered in the ordinary way.*

* Dr. A. Lauguard has described a species of aconite root, named by the Japanese *Kusa-usū*. From his experiments on frogs and rabbits, its physiological action seems not to differ from that of aconitine generally. *Über eine Art Japanische Aconit-knollen, Kusa-usū genannt, u. über das in denselben vorkommende Aconitin.* *Virchow's Archiv.* B. 79, p. 292, 1880.



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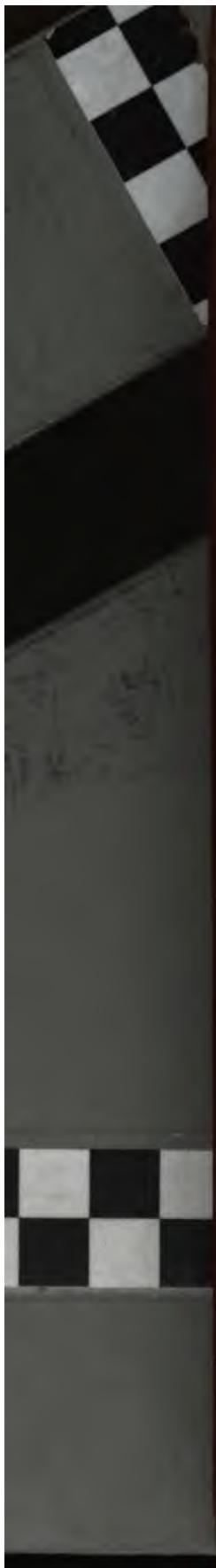
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